(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 April 2004 (15.04.2004)

PCT

(10) International Publication Number
WO 2004/031232 A1

(51) International Patent Classification[7]: C07K 14/475

(21) International Application Number:
PCT/AU2003/001310

(22) International Filing Date: 6 October 2003 (06.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2002951853 4 October 2002 (04.10.2002) AU

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CRYSTAL STRUCTURE OF ERBB2 AND USES THEREOF

(57) Abstract: More particularly, the present invention relates to the crystal structure of the ErbB2, in particular the crystal structure of an extracellular portion of ErbB2 and to methods of using the crystal and related structural information to screen for and design compounds that interact with ErbB2, or variants of thereof.

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Crystal Structure Of ErbB2 And Uses Thereof

Field of the invention

The present invention relates generally to structural studies of ErbB2. More particularly, the present invention relates to the crystal structure of the ErbB2, in particular the crystal structure of an extracellular portion of ErbB2 and to methods of using the crystal and related structural information to screen for and design compounds that interact with or modulate ErbB2; or variants thereof.

Background to the invention

ErbB2 was discovered as an oncogene (neu) in a rat brain tumor (Schecter et al., 1984, Nature 312, 513-516). ErbB2/HER2 is closely related to the EGF receptor and is the most oncogenic member of the EGFR family. It is amplified and/or overexpressed in approximately 30% of human breast cancers and in many other types of human malignancies and this overexpression is correlated with poor clinical prognosis (see Mendelsohn and Baselga, 2000, Oncogene 19, 6550-6565; Yu and Hung, 2000, Oncogene 19, 6115-6121). Overexpression of ErbB2 enhances metastasis-related properties such as invasion, angiogenesis and increased survival of cancer cells, and confers increased resistance to various cancer therapies including chemotherapy and gamma-radiation (see Mendelsohn and Baselga, 2000; Yu and Hung, 2000). Some forms of breast cancer are now treated with antibodies that recognise ErbB2 and improvements in anti-ErbB2 therapies are likely to flow from a better understanding of its 3D structure and its mechanism of action.

Considerable resources have been directed to the identification of an ErbB2 ligand. No ligand has been found, however the search led to the discovery of ErbB4 and considerable improvements in our biological understanding of the EGF receptor family (Harari and Yarden, 2000, Oncogene 19, 6102-6114; Yarden and Sliwkowski, 2001, Nat. Rev. Mol. Cell. Biol. 2, 127-137). It now seems certain that ErbB2 has no ligand. Instead it acts as a second receptor sub-unit in three EGF receptor family heterodimers: ErbB1-ErbB2, ErbB3-ErbB2 and ErbB4-ErbB2 (Daly et al., 1997, Cancer Res. 57, 3804-3811; Sundaresan et al., 1998, Endocrinol. 139, 4756-4764). There is definitive evidence that the EGF receptor homodimer signals differently to the EGF receptor-

ErbB2 heterodimer. Unless ErbB2 carries an oncogenic mutation, as in c-neu, it signals only after activation of its heterodimer partner by EGF or other relevant ligand.

The human ErbB2 is a large (1234 residues), monomeric, modular glycoprotein with an extracellular domain, a single transmembrane region and an intracellular cytoplasmic tyrosine kinase, which is flanked by noncatalytic regulatory regions (Yamamoto et al., 1986, Nature 319, 230-234). The extracellular portion of human ErbB2 (residues 1-632), like the EGFR, consists of four sub-domains L1, CR1, L2 and CR2 (Bajaj et al., 1987, Biochim. Biophys. Acta 916, 220-226; Ward et al., 1995, Proteins: Struct. Funct. Genet. 22, 141-153) also referred to as domains I-IV (Lax et al., 1988, Mol. Cell. Biol. 8, 1970-1978).

Summary of the invention

We have determined the three dimensional structure of a truncated form (residues 1-509) of the ectodomain of the tyrosine kinase receptor ErbB2 at 2.5 Å resolution and compared it with the recently solved structures of the EGFR ectodomain with TGFα or EGF and the unliganded ErbB3 ectodomain. Lack of ligand binding by ErbB2 appears to be caused by amino acid differences in the L1 and L2 domains of ErbB2. Furthermore, ligands would not be able to bind to the observed conformation of ErbB2 here as kinks in the first Cys-rich region (CR1) lead to a closer juxtaposition of the L domains, occluding the region of ErbB2 that is analogous to the EGFR ligand binding site. The L1/L2 buried surface area and the degree of complementarity in the L domain interface implies that this "closed" form is biologically relevant.

Accordingly, in one aspect, the present invention provides a method for identifying a potential modulator compound for ErbB2 which method comprises:

(a) providing a three-dimensional structure of

(i) amino acids 1-509 of ErbB2 polypeptide having the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or

(ii) a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the

corresponding backbone atoms described by the atomic coordinates shown in Appendix I;

(b) providing the three-dimensional structure of a candidate compound;

(c) assessing the stereochemical complementarity between the three-dimensional structure of step (b) and a region of the three-dimensional structure of step (a); and

(d) selecting a compound on the basis of the stereochemical complementarity.

In a preferred embodiment, the method further comprises:

(e) synthesising or obtaining a candidate compound assessed in step (c) as possessing stereochemical complementarity with the three-dimensional structure of step (a);

(f) determining the ability of the candidate compound to interact with and/or modulate the activity of ErbB2.

In yet a further aspect the present invention provides a method for preparing a pharmaceutical composition for treating diseases associated with aberrant ErbB2 signalling, the method comprising:

(a) providing a three-dimensional structure of

(i) amino acids 1-509 of ErbB2 polypeptide having the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or

(ii) a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I;

(b) providing the three-dimensional structure of a candidate compound;

(c) assessing the stereochemical complementarity between the three-dimensional structure of step (b) and a region of the three-dimensional structure of step (a); and

(d) selecting a compound on the basis of the stereochemical complementarity;

(e) synthesising or obtaining a candidate compound assessed in step (c) as possessing stereochemical complementarity with the three-dimensional structure of step (a);

(f) determining the ability of the candidate compound to interact with and/or modulate the activity of ErbB2; and

(g) incorporating the compound into a pharmaceutical composition.

The method may be used for either targeted or broad screening. Targeted screening involves the design and synthesis of chemical compounds that are analogs of some active compounds or that can specifically act with the biological target under investigation. Broad screening involves the design and synthesis of a large array of maximally diverse chemical compounds, leading to diverse libraries that are tested against a variety of biological targets.

In a further aspect, the present invention provides a method of modulating ErbB2, the method comprising contacting the receptor with a compound that matches a region selected from at least one of the CR1 domain, the potential CR1 loop docking site between the L1, CR1 and L2 domains, the CR1-L2 hinge region, the regions of the L1 and L2 domains that contact each other in a closed conformation.

The compound may be a small molecule modulator. The term "small molecule" includes an organic compound either synthesized in the laboratory or found in nature. Typically, a small molecule is any organic molecule having a molecular weight of less than about 1500. Preferably the molecule has a molecular weight less that about 1000, more preferably less than about 500.

The term "ErbB2" as used herein includes wild-type ErbB2 and variants thereof including allelic variants and naturally occurring mutations and genetically engineered variants.

The present invention also provides a set of coordinates as shown in Appendix I, or a subset thereof, where said coordinates define a three dimensional structure of amino acids 1-509 of an ErbB2 polypeptide or a subset of said amino acids, or a set of coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I, or a subset thereof.

In a related aspect, the present invention provides a computer for producing a three-dimensional representation of a molecule or molecular complex, wherein the computer comprises:

(a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein the machine readable data comprises (i) the atomic coordinates of amino acids 1-509 of an ErbB2 polypeptide as shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or (ii) the atomic coordinates of a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I;

(b) a working memory for storing instructions for processing the machine-readable data;

(c) a central-processing unit coupled to the working memory and to the machine-readable data storage medium, for processing the machine-readable data into the three dimensional representation; and

(d) an output hardware coupled to the central processing unit, for receiving the three-dimensional representation.

Preferably, said subsets of amino acids are selected from the CR1 domain and the potential CR1 loop docking site between the L1, CR1 and L2 domains equivalent to that seen in the TGFα:sEGFR dimer complex (Garrett et al., 2002, Cell 110, 763-773), or the CR1-L2 hinge region or the regions of the L1 and L2 domains that contact each other in this closed conformation.

More preferably the subset of amino acids defines a homodimerisation or heterodimerisation surface with other EGF receptor family members. Preferred heterodimerisation surfaces include (i) the N-terminal end of the CR1 domain (residues 200-203, 210-213, 216-218, 225-230), (ii) the CR1 domain dimerisation loop (residues 247-268) and adjacent residues (residues 244-246, 285-289) and (iii) the C-terminal end of the CR1 domain (residues 294-319).

In a further preferred embodiment, the subset of amino acids comprises the following residues: Gln 36, Gln 60, Arg 82, Thr 84, Gln 85, Phe 237, Thr 269, Phe 270, Gly 271, Ala 272, Tyr 282, Thr 285, Gly 288, Ser 289, Cys 290, Thr 291, Leu 292, Val 293, Cys 294, Pro 295 and Cys 310.

The three-dimensional structure of ErbB2 may be used to develop models useful for drug design and *in silico* screening of candidate compounds that modulate ErbB2 activity. Other physicochemical characteristics may also be used in developing the model, e.g. bonding, electrostatics etc.

Generally the term "*in silico*" refers to the creation in a computer memory, i.e., on a silicon or other like chip. Stated otherwise "*in silico*" means "virtual." When used herein the term "*in silico*" is intended to refer to screening methods based on the use of computer models rather than *in vitro* or *in vivo* experiments.

By "modulate" we mean that the compound increases or decreases signal transduction via ErbB2. The phrase "decreases signal transduction" is intended to encompass partial or complete inhibition of signal transduction via ErbB2. The ability of a candidate compound to increase or decrease signal transduction via ErbB2 can be assessed by any one of the ErbB2 cell-based assays described herein.

The term "small molecule" includes a compound with a molecular weight of 1500 or less. Preferably, the small molecule has a molecular weight of less than 1000, particularly preferred is a molecule having a molecular weight of less than 500.

Accordingly, in yet a further aspect, the present invention provides a computer-based method of identifying a candidate modulator of ErbB2, which method comprises fitting the structure of

(i) amino acids 1-509 of an ErbB2 polypeptide having the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or

(ii) a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I;

to the structure of a candidate modulator molecule.

In a further related aspect, the present invention provides a computer-assisted method for identifying candidate compounds able to interact with ErbB2 and thereby modulate an activity mediated by the receptor, using a programmed computer comprising a processor, an input device, and an output device, which method comprises the steps of:

(a) entering into the programmed computer, through the input device, data comprising the atomic coordinates of amino acids 1-509 of ErbB2 as shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I, or a subset of said coordinates;

(b) generating, using computer methods, a set of atomic coordinates of a structure that possesses stereochemical complementarity to the atomic coordinates entered in step (a), thereby generating a criteria data set;

(c) comparing, using the processor, the criteria data set to a computer database of chemical structures;

(d) selecting from the database, using computer methods, chemical structures which are similar to a portion of said criteria data set; and

(e) outputting, to the output device, the selected chemical structures which are complementary to or similar to a portion of the criteria data set.

In another related aspect, the present invention provides a method for evaluating the ability of a chemical entity to interact with an ErbB2, said method comprising the steps of:

(a) providing a computer model of at least one region of ErbB2 using structure coordinates wherein the root mean square deviation between said structure coordinates and the structure coordinates of amino acids 1-509 of ErbB2 as set forth in Appendix I is not more than 1.5 Å;

(b) employing computational means to perform a fitting operation between the chemical entity and said computer model of the binding surface; and

(c) analysing the results of said fitting operation to quantify the association between the chemical entity and the binding surface model.

The model may be adaptive in a sense that it allows for slight surface changes to improve the fit between the candidate compound and the protein , e.g. by small movements in side chains or main chain.

Preferably, the region of ErbB2 is defined by the CR1 domain and the potential CR1 loop docking site between the L1, CR1 and L2 domains equivalent to that seen in the TGFα:sEGFR dimer complex (Garrett et al., 2002), or the CR1-L2 hinge region or the regions of the L1 and L2 domains that contact each other in this closed conformation and combinations thereof.

More preferably the region defines a heterodimerisation surface with other EGF receptor family members. Preferred heterodimerisation surfaces include (i) the N-terminal end of the CR1 domain (residues 200-203, 210-213, 216-218, 225-230), (ii) the CR1 domain dimerisation loop (residues 247-268) and adjacent residues (residues 244-246, 285-289) and (iii) the C-terminal end of the CR1 domain (residues 294-319).

In a further preferred embodiment, the region comprises the following amino acid residues: Gln 36, Gln 60, Arg 82, Thr 84, Gln 85, Phe 237, Thr 269, Phe 270, Gly 271, Ala 272, Tyr 282, Thr 285, Gly 288, Ser 289, Cys 290, Thr 291, Leu 292, Val 293, Cys 294, Pro 295 and Cys 310.

The ErbB2 crystal structure provided herein may also be used to model/solve the structure of a new crystal using molecular replacement. Accordingly, in a further aspect the present invention provides a method of using molecular replacement to obtain structural information about a molecule or a molecular complex of unknown structure, comprising the steps of:

(i) crystallising said molecule or molecular complex;

(ii) generating an X-ray diffraction pattern from said crystallized molecule or molecular complex;

(iii) applying at least a portion of the structure coordinates set forth in Appendix I, or structure coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the structure coordinates set forth in Appendix I, to the X-ray diffraction pattern to generate a three-dimensional electron density map of at least a portion of the molecule or molecular complex whose structure is unknown.

Preferably the molecule of unknown structure is ErbB2 or variant thereof.

In one embodiment, the molecular complex of unknown structure is a complex of ErbB2, or variant thereof, and a ligand or candidate ligand.

In another embodiment the molecular complex of unknown structure is a complex of ErbB2 and an EGF receptor. The molecular complex of unknown structure may also be a complex of ErbB2, an ErbB1 (EGF receptor), ErbB3 or ErbB4 receptor and a ligand or candidate ligand.

The screening methods of the fourth aspect of the invention may be used to identify compounds that modulate ErbB2 signalling. Such compounds may be used to treat disorders associated with ErbB2 dysfunction.

Accordingly, in a further aspect, the present invention provides a method for preventing or treating a disease associated with signaling by ErbB2 which method comprises administering to a subject in need thereof a compound identified by the screening methods of the invention.

The present invention also provides a pharmaceutical composition comprising a compound identified by the screening methods of the invention, which compound is able to bind to the extracellular domain of ErbB2 and modulate an activity of said receptor, as well as a method of preventing or treating a disease associated with signalling by ErbB2 which method comprises administering to a subject in need thereof a composition of the invention.

In yet a further aspect, the present invention provides a crystal of an ErbB2 polypeptide. In particular the present invention provides a crystal of an ErbB2 polypeptide having a space group $P2_12_12_1$ with unit cell dimensions of a=75.96 Å, b=82.24 Å, and c=110.06 Å with up to about 1% variation in any cell dimension. Preferably said ErbB2 polypeptide is a truncated soluble extracellular domain of the full-length ErbB2.

The present invention also provides a crystalline composition comprising a crystal of ErbB2.

In a further aspect, the invention provides a computer system for identifying one or more candidate modulators of ErbB2, the system containing data representing the structure of

(i) amino acids 1-509 of ErbB2 polypeptide having the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or

(ii) a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I.

The present invention further provides a computer readable media having recorded thereon data representing a model and/or the atomic coordinates of a ErbB2 crystal. Also provided is a computer readable media having recorded thereon coordinate data according to Appendix I, or a subset thereof, where said coordinate data define a three dimensional structure of amino acids 1-509 of ErbB2 polypeptide or a subset of said amino acids, or coordinate data having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinate according to Appendix I, or a subset thereof.

Particular diseases associated with signalling by ErbB2 include cancerous conditions such as cancer of the brain, head and neck, prostate, testicular, ovary, breast, cervix, lung, pancreas and colon; and melanoma, rhabdomyosarcoma, mesothelioma, squamous carcinomas of the skin and glioblastoma.

The information provided in Appendix I shows that there are a number of loop structures that line the ErbB2 dimerisation surface. It is envisaged that antibodies directed against these loop structures would interfere with the formation of heterodimers with other members of the EGF receptor family.

Accordingly, in a further aspect the present invention provides an antibody that binds to ErbB2, the antibody being directed against a structure defined by (i) ErbB2 amino acid residues 200-203, (ii) ErbB2 amino acid residues 210-213, (iii) ErbB2 amino acid residues 216-218, (iv) ErbB2 amino acid residues 225-230, (v) ErbB2 amino acid

residues 247-268 or a subset thereof; (vi) ErbB2 amino acid residues 244-246, (vii) ErbB2 amino acid residues 285-289, or (viii) ErbB2 amino acid residues 294-319 or a subset thereof.

In yet a further aspect the present invention provides an isolated conformationally constrained peptide or peptidomimetic consisting essentially of (i) ErbB2 amino acid residues 200-203, (ii) ErbB2 amino acid residues 210-213, (iii) ErbB2 amino acid residues 216-218, (iv) ErbB2 amino acid residues 225-230, (v) ErbB2 amino acid residues 247-268 or a subset thereof; (vi) ErbB2 amino acid residues 244-246, (vii) ErbB2 amino acid residues 285-289, or (viii) ErbB2 amino acid residues 294-319 or a subset thereof.

In yet a further aspect the present invention provides a computer-assisted method for identifying potential mimetics of ErbB2, using a programmed computer comprising a processor, a data storage system, an input device, and an output device, comprising the steps of:

(a) inputting into the programmed computer through said input device data comprising the atomic coordinates of amino acids 200-203, 210-213, 216-218, 225-230, 247-268, 244-246, 285-289, or 294-319 of ErbB2 as shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I, thereby generating a criteria data set;

(b) comparing, using said processor, said criteria data set to a computer database of chemical structures stored in said computer data storage system;

(c) selecting from said database, using computer methods, chemical structures having a portion that is structurally similar to said criteria data set;

(d) outputting to said output device the selected chemical structures having a portion similar to said criteria data set.

In yet a further aspect the present invention provides a computer-assisted method for identifying potential mimetics of ErbB2, using a programmed computer comprising a processor, a data storage system, an input device, and an output device, comprising the steps of:

(a) inputting into the programmed computer through said input device data comprising the atomic coordinates of amino acids 200-203, 210-213, 216-218, 225-230, 247-268, 244-246, 285-289, or 294-319 of ErbB2 as shown in Appendix I, or atomic coordinates

having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I, thereby generating a criteria data set;

(b) constructing, using computer methods, a model of a chemical structure having a portion that is structurally similar to said criteria data set;

(c) outputting to said output device the constructed model.

In yet a further aspect the present invention provides a compound having a chemical structure selected using a method of the present invention, said compound being an ErbB2 mimetic. Preferably, the compound is a peptidomimetic that has fewer than 30 amino acids, more preferably fewer than 25 amino acids.

As will be readily understood by those skilled in this field the methods of the present invention provide a rational method for designing and selecting compounds including antibodies which interact with ErbB2. In the majority of cases these compounds will require further development in order to increase activity. Such further development is routine in this field and will be assisted by the structural information provided in this application. It is intended that in particular embodiments the methods of the present invention includes such further developmental steps.

It is also intended that embodiments of the present invention include manufacturing steps such as incorporating the compound into a pharmaceutical composition in the manufacture of a medicament.

Throughout this specification, preferred aspects and embodiments apply, as appropriate, separately, or in combination, to other aspects and embodiments, mutatis mutandis, whether or not explicitly stated as such.

Brief Description of the Figures

Figure 1. Structure-based sequence alignment of the human ErbB2 ectodomain with other members of the ErbB family.

(A) The receptor L1 and L2 domains plus the first module of the cys-rich regions, CR1 and CR2. Positions with conserved physicochemical properties of amino acids are boxed. Disulfide bond connections are shown are solid lines. Secondary structure

elements are indicated above and below the sequences as cylinders for α-helices and arrows for β-strands. Residues buried at L1/L2 interface are denoted by R. Sequence sources are: EGFR (Ullrich et al., 1984, Nature 309, 418-425), ErbB2 (Yamamoto et al., 1986); ErbB3 (Kraus et al., 1989, Proc Natl Acad Sci U S A. 86, 9193-9197; Plowman et al., 1990, Proc. Natl Acad. Sci. U S A. 87, 4905-4909); ErbB4 (Plowman et al., 1993, Proc. Natl. Acad. Sci. USA. 90, 1746-1750).

(B) Modules 2 to 8 of the ErbB family cys-rich region CR1 and modules 2 to 7 of CR2. Three types of disulfide bonded modules are indicated by bars below the sequences. The unfilled bars below parts of the cys-rich sequences indicate modules with 2 disulfide bonds (in a Cys 1-3 and 2-4 arrangement), the solid bars indicate modules which contain a single disulfide bond and have a β-finger motif, and the dashed bar indicates residues present in a disulfide-linked bend consisting of only five residues. Disulfide bonds are shown in solid lines and except for those that do not conform to the CR1 pattern which are indicated as dashed lines. The number in parentheses shows where amino acids have been omitted. Boxed residues and secondary structure elements are as in A.

Figure 2. Polypeptide fold for residues 1-509 of ErbB2 and its comparison with EGFR (1-501) as seen in the 2:2 complex with TGFα, and the full length ectodomain of ErbB3.

Figure 3. Percentage inhibition of thymidine incorporated in a cell line expressing erbB2 on EGFR-K721R (a kinase defective EGFR) + full length ErbB2 by compounds 39293, 94289, 19378 and 20697.

Detailed description of the invention

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art (e.g. in molecular biology, biochemistry, structural biology, and computational biology). Standard techniques are used for molecular and biochemical methods (see generally, Sambrook et al., Molecular Cloning: A Laboratory Manual, 3rd ed. (2001) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. and Ausubel et al., Short Protocols in Molecular Biology (1999) 4th Ed, John Wiley & Sons, Inc. - and the full version

entitled Current Protocols in Molecular Biology, which are incorporated herein by reference) and chemical methods.

Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

ErbB2 crystals and crystal structures

The present invention provides a crystal comprising an ErbB2 polypeptide. Such crystals preferably are of the space group $P2_12_12_1$ with unit cell dimensions of a=75.96 Å, b=82.24 Å, and c=110.06 Å.

As used herein, the term "crystal" means a structure (such as a three dimensional (3D) solid aggregate) in which the plane faces intersect at definite angles and in which there is a regular structure (such as internal structure) of the constituent chemical species. Thus, the term "crystal" can include any one of: a solid physical crystal form such as an experimentally prepared crystal, a 3D model based on the crystal structure, a representation thereof such as a schematic representation thereof or a diagrammatic representation thereof, a data set thereof for a computer.

Crystals according to the invention may be prepared using full-length ErbB2 polypeptides. However, preferably the extracellular domain is employed in isolation. Thus, preferably the ErbB2 polypeptide is a truncated polypeptide containing the extracellular domain and lacking the transmembrane domain and the intracellular tyrosine kinase domain. Typically, the extracellular domain comprises residues 1 to 632 (mature receptor numbering) of human ErbB2, or the equivalent thereof, or a truncated version thereof, preferably comprising amino acids 1 to 509, or the equivalent residues in other ErbB2 polypeptides.

In a preferred embodiment the ErbB2 polypeptide is human ErbB2 (Accession No. A24571 – mature protein begins at residue 22). However, the ErbB2 polypeptide may also be obtained from other species, such as other mammalian species.

Crystals may be constructed with wild-type ErbB2 polypeptide sequences or variants thereof, including allelic variants and naturally occurring mutations as well as genetically engineered variants. Typically, variants have at least 95 or 98% sequence identity with a corresponding wild-type ErbB2 polypeptide.

Optionally, the crystal of ErbB2 may comprise one or more molecules which bind to ErbB2, or otherwise soaked into the crystal or cocrystallise with ErbB2. Such molecules include ligands or small molecules, which may be candidate pharmaceutical agents intended to modulate the interaction between ErbB2 and its biological targets or dimer partners, such as other members of the EGF receptor family. The crystal of ErbB2 may also be a molecular complex with other receptors of the EGF receptor family such as ErbB1 (the EGF receptor), ErbB3 or ErbB4. The complex may also comprise additional molecules such as the ligands to these receptors.

The production of ErbB2 crystals is described below.

In a preferred embodiment, an ErbB2 crystal of the invention has the atomic coordinates set forth in Appendix I. It will be understood by those skilled in the art that atomic coordinates may be varied, without affecting significantly the accuracy of models derived therefrom; thus, although the invention provides a very precise definition of a preferred atomic structure, it will be understood that minor variations are envisaged and the claims are intended to encompass such variations. Preferred are variants in which the r.m.s. deviation of the x, y and z co-ordinates for all backbone atoms other than hydrogen is less than 1.5 Å (preferably less than 1 Å, 0.7 Å or less than 0. 3 Å) compared with the coordinates given in Appendix I.

In a highly preferred embodiment, the crystal has the atomic coordinates as shown in Appendix I.

As used herein, the term "atomic co-ordinates" refer to a set of values which define the position of one or more atoms with reference to a system of axes.

The present invention also provides a crystal structure of an ErbB2 polypeptide, in particular a crystal structure of the extracellular domain of an ErbB2 polypeptide, or a region thereof.

The atomic coordinates obtained experimentally for amino acids 1 to 509 (mature receptor numbering) of human ErbB2 are shown in Appendix I. However, a person skilled in the art will appreciate that a set of atomic coordinates determined by X-ray crystallography is not without standard error. Accordingly, any set of structure coordinates for an ErbB2 polypeptide that has a root mean square deviation of protein backbone atoms of less than 0.75 Å when superimposed (using backbone atoms) on the atomic coordinates listed in Appendix I shall be considered identical.

The present invention also comprises the atomic coordinates of an ErbB2 polypeptide that substantially conform to the atomic coordinates listed in Appendix I.

A structure that "substantially conforms" to a given set of atomic coordinates is a structure wherein at least about 50% of such structure has an average root-mean-square deviation (RMSD) of less than about 1.5 Å for the backbone atoms in secondary structure elements in each domain, and more preferably, less than about 1.3 Å for the backbone atoms in secondary structure elements in each domain, and, in increasing preference, less than about 1.0 Å, less than about 0.7 Å, less than about 0.5 Å, and most preferably, less than about 0.3 Å for the backbone atoms in secondary structure elements in each domain.

In a more preferred embodiment, a structure that substantially conforms to a given set of atomic coordinates is a structure wherein at least about 75% of such structure has the recited average root-mean-square deviation (RMSD) value, and more preferably, at least about 90% of such structure has the recited average root-mean-square deviation (RMSD) value, and most preferably, about 100% of such structure has the recited average root-mean-square deviation (RMSD) value.

In an even more preferred embodiment, the above definition of "substantially conforms" can be extended to include atoms of amino acid side chains. As used herein, the phrase "common amino acid side chains" refers to amino acid side chains that are common to both the structure which substantially conforms to a given set of atomic coordinates and the structure that is actually represented by such atomic coordinates.

The present invention also provides subsets of said atomic coordinates listed in Appendix I and subsets that conform substantially thereto. Preferred subsets define one or more regions of the human ErbB2 extracellular domain selected from the CR1

domain and the potential CR1 loop docking site between the L1, CR1 and L2 domains equivalent to that seen in the TGFα:sEGFR dimer complex (Garrett et al., 2002), or the CR1-L2 hinge region or the regions of the L1 and L2 domains that contact each other in this closed conformation. A particularly preferred subset defines the heterodimerisation surface of ErbB2 with other members of the EGF receptor family, such as ErbB1, ErbB3 and/or ErbB4.

It will be appreciated that a set of structure coordinates for a polypeptide is a relative set of points that define a shape in three dimensions. Thus, it is possible that an entirely different set of coordinates could define a similar or identical shape. Moreover, slight variations in the individual coordinates will have little effect on overall shape.

The variations in coordinates may be generated due to mathematical manipulations of the structure coordinates. For example, the structure coordinates set forth in Appendix I could be manipulated by crystallographic permutations of the structure coordinates, fractionalisation of the structure coordinates, integer additions or subtractions to sets of the structure coordinates, inversion of the structure coordinates, or any combination thereof.

Alternatively, modification in the crystal structure due to mutations, additions, substitutions, and/or deletions of amino acids, or other changes in any of the components that make up the crystal could also account for variations in structure coordinates.

Various computational analyses are used to determine whether a molecular complex or a portion thereof is sufficiently similar to all or parts of the structure of the extracellular domain of ErbB2 described above. Such analyses may be carried out in current software applications, such as the Molecular Similarity program of QUANTA (Molecular Simulations Inc., San Diego, CA) version 4.1.

The Molecular Similarity program permits comparisons between different structures, different conformations of the same structure, and different parts of the same structure.

Comparisons typically involve calculation of the optimum translations and rotations required such that the root mean square difference of the fit over the specified pairs of equivalent atoms is an absolute minimum. This number is given in angstroms.

Accordingly, structural coordinates of an ErbB2 within the scope of the present invention include structural coordinates related to the atomic coordinates listed in Appendix I by whole body translations and/or rotations. Accordingly, r.m.s deviations listed above assume that at least the backbone atoms of the structures are optimally superimposed which may require translation and/or rotation to achieve the required optimal fit from which to calculate the r.m.s.d.

A three dimensional structure of an ErbB2 protein or region thereof which substantially conforms to a specified set of atomic coordinates can be modeled by a suitable modeling computer program such as MODELER (Sali and Blundell, 1993, J. Mol. Biol., vol. 234:779-815), as implemented in the Insight II Homology software package (Insight II (97.0), MSI, San Diego)), using information, for example, derived from the following data: (1) the amino acid sequence of the human ErbB2 protein; (2) the amino acid sequence of the related portion(s) of the protein represented by the specified set of atomic coordinates having a three dimensional configuration; and, (3) the atomic coordinates of the specified three dimensional configuration. A three dimensional structure of an ErbB2 protein which substantially conforms to a specified set of atomic coordinates can also be calculated by a method such as molecular replacement, which is described in detail below.

Structure coordinates/atomic coordinates are typically loaded onto a machine readable-medium for subsequent computational manipulation. Thus models and/or atomic coordinates are advantageously stored on machine-readable media, such as magnetic or optical media and random-access or read-only memory, including tapes, diskettes, hard disks, CD-ROMs and DVDs, flash memory cards or chips, servers and the internet. The machine is typically a computer.

The structure coordinates/atomic coordinates may be used in a computer to generate a representation, e.g. an image, of the three-dimensional structure of the ErbB2 crystal which can be displayed by the computer and/or represented in an electronic file.

The structure coordinates/atomic coordinates and models derived therefrom may also be used for a variety of purposes such as drug discovery and X-ray crystallographic analysis of other protein crystals.

Design/selection of chemical entities that bind ErbB2

Using a variety of known modelling techniques, the crystal structure of the present invention can be used to produce a model for at least part of ErbB2 .

As used herein, the term "modelling" includes the quantitative and qualitative analysis of molecular structure and/or function based on atomic structural information and interaction models. The term "modelling" includes conventional numeric-based molecular dynamic and energy minimisation models, interactive computer graphic models, modified molecular mechanics models, distance geometry and other structure-based constraint models.

Molecular modelling techniques can be applied to the atomic coordinates of the ErbB2 to derive a range of 3D models and to investigate the structure of binding sites, such as the binding sites of monoclonal antibodies and inhibitory peptides.

These techniques may also be used to screen for or design small and large chemical entities which are capable of binding ErbB2 and modulating the ability of ErbB2 to interact with extracellular biological targets, such as other members of the EGF receptor family e.g. which modulate the ability of ErbB2 to heterodimerise. The screen may employ a solid 3D screening system or a computational screening system.

Such modelling methods are to design or select chemical entities that possess stereochemical complementary to particular regions of ErbB2.

By "stereochemical complementarity" we mean that the compound or a portion thereof makes a sufficient number of energetically favourable contacts with the receptor as to have a net reduction of free energy on binding to the receptor.

Such stereochemical complementarity is characteristic of a molecule that matches intra-site surface residues lining the groove of the receptor site as enumerated by the coordinates set out in Appendix I. By "match" we mean that the identified portions interact with the surface residues, for example, via hydrogen bonding or by non-covalent Van der Waals and Coulomb interactions (with surface or residue) which promote desolvation of the molecule within the site, in such a way that retention of the molecule within the groove is favoured energetically.

It is preferred that the stereochemical complementarity is such that the compound has a K_d for the receptor site of less than 10^{-4}M, more preferably less than 10^{-5}M and more preferably 10^{-6}M. In a most preferred embodiment, the K_d value is less than 10^{-8}M and more preferably less than 10^{-9}M.

Chemical entities which are complementary to the shape and electrostatics or chemistry of the receptor site characterised by amino acids positioned at atomic coordinates set out in Appendix I will be able to bind to the receptor, and when the binding is sufficiently strong, substantially prohibit the interaction of the ErbB2 with biological target molecules such as other EGF receptors.

It will be appreciated that it is not necessary that the complementarity between chemical entities and the receptor site extend over all residues lining the groove in order to inhibit binding of a molecule or complex that naturally interacts with ErbB2.

A number of methods may be used to identify chemical entities possessing stereo-complementarity to a region of the extracellular domain of ErbB2. For instance, the process may begin by visual inspection of potential binding sites, for example, the binding sites for anti- ErbB2 antibodies, on the computer screen based on the ErbB2 coordinates in Appendix I generated from the machine-readable storage medium. Alternatively, selected fragments or chemical entities may then be positioned in a variety of orientations, or docked, within an individual binding site of ErbB2, as defined *supra*. Modelling software that is well known and available in the art may be used (Guida, W. C. (1994). "Software For Structure-Based Drug Design." Curr. Opin. Struct. Biology 4: 777-781). These include QUANTA and InsightII [Molecular Simulations, Inc., San Diego, Calif., a division of Pharmacopiea, Inc., Princeton, N.J., 1992], SYBYL [Molecular Modeling Software, Tripos Associates, Inc., St. Louis, Mo., 1992], This modelling step may be followed by energy minimization with standard molecular mechanics force fields such as AMBER [S. J. Weiner, P. A. Kollman, D. A. Case, U. C. Singh, C. Ghio, G. Alagona, and P. Weiner, J. Am. Chem. Soc., vol. 106, pp. 765-784 (1984)], and CHARMM [B. R. Brooks, R. E. Bruccoleri, B. D. Olafson, D. J. States, S Swaminathan, and M. Karplus, J. Comp. Chem. vol. 4, pp. 187-217 (1983)]. In addition, there are a number of more specialized computer programs to assist in the process of selecting the binding moieties of this invention.

Specialised computer programs may also assist in the process of selecting fragments or chemical entities. These include, inter alia:

1. GRID (Goodford, P. J.,"A Computational Procedure for Determining Energetically Favorable Binding Sites on Biologically Important Macromolecules", J. Med. Chem., 28, pp. 849-857 (1985)). GRID is available from Oxford University, Oxford, UK.

2. MCSS (Miranker, A. and M. Karplus, "Functionality Maps of Binding Sites: A Multiple Copy Simultaneous Search Method. "Proteins: Structure, Function and Genetics, 11, pp. 29-34 (1991)). MCSS is available from Molecular Simulations, Burlington, MA.

3. AUTODOCK (Goodsell, D. S. and A. J. Olsen, "Automated Docking of Substrates to Proteins by Simulated Annealing", Proteins: Structure, Function, and Genetics, 8, pp. 195-202 (1990)). AUTODOCK is available from Scripps Research Institute, La Jolla, CA.

4. DOCK (Kuntz, I. D. et al.,"A Geometric Approach to Macromolecule-Ligand Interactions", J. Mol. Biol., 161, pp. 269-288 (1982)). DOCK is available from University of California, San Francisco, CA.

Once suitable chemical entities or fragments have been selected, they can be assembled into a single compound. In one embodiment, assembly may proceed by visual inspection of the relationship of the fragments to each other on the three-dimensional image displayed on a computer screen in relation to the structure coordinates of ErbB2. This is followed by manual model building using software such as Quanta or Sybyl. Alternatively, fragments may be joined to additional atoms using standard chemical geometry.

The above-described evaluation process for chemical entities may be performed in a similar fashion for chemical compounds.

Useful programs to aid one of skill in the art in connecting the individual chemical entities or fragments include:

1. CAVEAT (Bartlett et al, "CAVEAT: A Program to Facilitate the Structure-Derived Design of Biologically Active Molecules". In "Molecular Recognition in Chemical and Biological Problems", Special Pub., Royal Chem. Soc., 78, pp. 182-196 (1989)). CAVEAT is available from the University of California, Berkeley, CA.

2. 3D Database systems such as MACCS-3D (MDL Information Systems, San Leandro, CA). This area is reviewed in Martin, "3D Database Searching in Drug Design", J. Med. Chem., 35, pp. 2145-2154 (1992)).

3. HOOK (available from Molecular Simulations, Burlington, MA).

Other molecular modeling techniques may also be employed in accordance with this invention. See, e. g., Cohen et al., "Molecular Modeling Software and Methods for Medicinal Chemistry", J. Med. Chem., 33, pp. 883-894 (1990). See also Navia and Murcko, "The Use of Structural Information in Drug Design", Current Opinions in Structural Biology, 2, pp. 202-210 (1992).

There are two preferred approaches to designing a molecule, according to the present invention, that complement the stereochemistry of ErbB2. The first approach is to in silico directly dock molecules from a three-dimensional structural database, to the receptor site, using mostly, but not exclusively, geometric criteria to assess the goodness-of-fit of a particular molecule to the site. In this approach, the number of internal degrees of freedom (and the corresponding local minima in the molecular conformation space) is reduced by considering only the geometric (hard-sphere) interactions of two rigid bodies, where one body (the active site) contains "pockets" or "grooves" that form binding sites for the second body (the complementing molecule).

This approach is illustrated by Kuntz et al., 1982, J. Mol. Biol. 161: 269, and Ewing et al., 2001, J. Comput-Aid. Mol. Design 15: 411, the contents of which are hereby incorporated by reference, whose algorithm for ligand design is implemented in a commercial software package, DOCK version 4.0, distributed by the Regents of the University of California and further described in a document, provided by the distributor, which is entitled "Overview of the DOCK program suite" the contents of which are hereby incorporated by reference. Pursuant to the Kuntz algorithm, the shape of the cavity represented by a site on ErbB2 is defined as a series of overlapping spheres of different radii. One or more extant databases of crystallographic data, such

as the Cambridge Structural Database System maintained by Cambridge University (University Chemical Laboratory, Lensfield Road, Cambridge, U.K.), the Protein Data Bank maintained by the Research Collaboratory for Structural Bioinformatics (Rutgers University, N.J., U.S.A.), LeadQuest (Tripos Associates, Inc., St. Louis, MO), Available Chemicals Directory (Molecular Design Ltd., San Leandro, CA), and the NCI database (National Cancer Institute, U.S.A) is then searched for molecules which approximate the shape thus defined.

Molecules identified on the basis of geometric parameters, can then be modified to satisfy criteria associated with chemical complementarity, such as hydrogen bonding, ionic interactions and Van der Waals interactions. Different scoring functions can be employed to rank and select the best molecule from a database. See for example Bohm and Stahl, 1999, M. Med. Chem. Res. 9: 445. The software package FlexX, marketed by Tripos Associates, Inc. (St. Louis, MO) is another program that can be used in this direct docking approach (see Rarey, M. et al., J. Mol. Biol. 1996, 261: 470).

The second preferred approach entails an assessment of the interaction of respective chemical groups ("probes") with the active site at sample positions within and around the site, resulting in an array of energy values from which three-dimensional contour surfaces at selected energy levels can be generated. The chemical-probe approach to ligand design is described, for example, by Goodford, 1985, J. Med. Chem. 28:849, the contents of which are hereby incorporated by reference, and is implemented in several commercial software packages, such as GRID (product of Molecular Discovery Ltd., West Way House, Elms Parade, Oxford OX2 9LL, U.K.).

Pursuant to this approach, the chemical prerequisites for a site-complementing molecule are identified at the outset, by probing the active site with different chemical probes, e.g., water, a methyl group, an amine nitrogen, a carboxyl oxygen, or a hydroxyl. Favoured sites for interaction between the active site and each probe are thus determined, and from the resulting three-dimensional pattern of such sites a putative complementary molecule can be generated. This may be done either by programs that can search three-dimensional databases to identify molecules incorporating desired pharmacophore patterns or by programs which using the favoured sites and probes as input to perform de novo design. Suitable programs for determining and designing pharmacophores include CATALYST (including HypoGen or HipHop) (Molecular

Simulations, Inc), and CERIUS2, DISCO (Abbott Laboratories, Abbott Park, IL) and ChemDBS-3D (Chemical Design Ltd., Oxford, U.K.).

The pharmacophore can be used to screen in silico compound libraries/ three-dimensional databases, using a program such as CATALYST (Molecular Simulations, Inc); MACCS-3D and ISIS/3D (Molecular Design Ltd., San Leandro, CA), ChemDBS-3D (Chemical Design Ltd., Oxford, U.K.), and Sybyl/3DB Unity (Tripos Associates, Inc., St. Louis, MO).

Databases of chemical structures are available from a number of sources including Cambridge Crystallographic Data Centre (Cambridge, U.K.), Molecular Design, Ltd., (San Leandro, CA), Tripos Associates, Inc. (St. Louis, MO), Chemical Abstracts Service (Columbus, OH), the Available Chemical Directory (MDL Inc), the Derwent World Drug Index (WDI), BioByteMasterFile, the National Cancer Institute database (NCI), and the Maybridge catalogue.

De novo design programs include LUDI (Biosym Technologies Inc., San Diego, CA), Leapfrog (Tripos Associates, Inc.), Aladdin (Daylight Chemical Information Systems, Irvine, CA), and LigBuilder (Peking University, China).

Once an entity or compound has been designed or selected by the above methods, the efficiency with which that entity or compound may bind to ErbB2 can be tested and optimised by computational evaluation. For example, a compound that has been designed or selected to function as an ErbB2 binding compound must also preferably traverse a volume not overlapping that occupied by the binding site when it is bound to the native ErbB2. An effective ErbB2 binding compound must preferably demonstrate a relatively small difference in energy between its bound and free states (i. e., a small deformation energy of binding). Thus, the most efficient ErbB2 binding compound should preferably be designed with a deformation energy of binding of not greater than about 10 kcal/mole, preferably, not greater than 7 kcal/mole. ErbB2 binding compounds may interact with ErbB2 in more than one conformation that is similar in overall binding energy. In those cases, the deformation energy of binding is taken to be the difference between the energy of the free compound and the average energy of the conformations observed when the compound binds to the protein.

A compound designed or selected as binding to ErbB2 may be further computationally optimised so that in its bound state it would preferably lack repulsive electrostatic interaction with the target protein.

Such non-complementary (e.g., electrostatic) interactions include repulsive charge-charge, dipole-dipole and charge-dipole interactions. Specifically, the sum of all electrostatic interactions between the compound and the protein when the compound is bound to ErbB2, preferably make a neutral or favourable contribution to the enthalpy of binding.

Once an ErbB2-binding compound has been optimally selected or designed, as described above, substitutions may then be made in some of its atoms or side groups to improve or modify its binding properties. Generally, initial substitutions are conservative, i. e., the replacement group will have approximately the same size, shape, hydrophobicity and charge as the original group. It should, of course, be understood that components known in the art to alter conformation should be avoided. Such substituted chemical compounds may then be analysed for efficiency of fit to ErbB2 by the same computer methods described in detail above.

Specific computer software is available in the art to evaluate compound deformation energy and electrostatic interaction. Examples of programs designed for such uses include: Gaussian 92, revision C (Frisch, Gaussian, Inc., Pittsburgh, PA) ; AMBER, version 4.0 (Kollman, University of California at San Francisco); QUANTA/CHARMM (Molecular Simulations, Inc., Burlington, MA); and Insight II/Discover (Biosysm Technologies Inc., San Diego, CA).

The screening/design methods may be implemented in hardware or software, or a combination of both. However, preferably, the methods are implemented in computer programs executing on programmable computers each comprising a processor, a data storage system (including volatile and non-volatile memory and/or storage elements), at least one input device, and at least one output device. Program code is applied to input data to perform the functions described above and generate output information. The output information is applied to one or more output devices, in known fashion. The computer may be, for example, a personal computer, microcomputer, or workstation of conventional design.

Each program is preferably implemented in a high level procedural or object-oriented programming language to communicate with a computer system. However, the programs can be implemented in assembly or machine language, if desired. In any case, the language may be compiled or interpreted language.

Each such computer program is preferably stored on a storage medium or device (e.g., ROM or magnetic diskette) readable by a general or special purpose programmable computer, for configuring and operating the computer when the storage media or device is read by the computer to perform the procedures described herein. The system may also be considered to be implemented as a computer-readable storage medium, configured with a computer program, where the storage medium so configured causes a computer to operate in a specific and predefined manner to perform the functions described herein.

Compounds identified by, or designed by the methods of the invention can be synthetic or naturally occurring, preferably synthetic. In one embodiment, a synthetic compound selected or designed by the methods of the invention preferably has a molecular weight equal to or less than about 5000 or 1000 daltons. A compound selected or designed by methods of this invention is preferably soluble under physiological conditions.

Confirmation of binding and biological activity

Compounds selected or designed in accordance with the in silico methods of the invention may be subjected to further confirmation of binding to ErbB2 by cocrystallization of the compound with ErbB2 and structural determination, as described herein.

Compounds designed or selected according to the methods of the present invention are preferably assessed by a number of *in vitro* and *in vivo* assays of ErbB2 function to confirm their ability to interact with and modulate ErbB2 activity. For example, compounds may be tested for their ability to bind to ErbB2 and/or for their ability to modulate e.g. disrupt, heterodimerisation of ErbB2 to other members of the EGF receptor family such as ErbB1, ErbB3 or ErbB4.

Suitable assays include *in vitro* binding assays and ErbB2-dependent proliferation assays, such as described by Deb et al., 2001, J Biol Chem 276:15554-15560 or Berezov et al., 2001, J. Med. Chem. 44: 2565-2574.

Particular examples of suitable assays are described below.

Inhibition of heterodimer formation between ErbB2 and other ErbB family members

Rationale: While ErB2 is a major oncogenic therapeutic target in its own right, it is now clear that part of the tumour-promoting activity associated with ErbB2 often depends on ligand-induced heterodimer formation with other ErbB family members. There is no known ligand for ErbB2, however ligand binding to other ErbB family members (ErbB1, ErbB3 and ErbB4) causes their heterodimerization with ErbB2. Thus reagents that block this association, for example the ErbB2-specific antibody 2C4, inhibit ligand-stimulated growth *in vitro* and tumour xenograft *in vivo* (Agus, D.B. et.al. Cancer Cell 2:127-137). Heterodimerization results in cross-phosphorylation by the ErbB2 kinase of the dimerization partner. In particular, ErbB3 mediated signalling requires heterodimer formation as this particular ErbB family member lacks a functional kinase. Thus, while it is not possible to directly ligand-activate the ErbB2 kinase, it is possible to monitor its activity in cells co-expressing ErbB2 with one or more members of the EGFR family by adding ligands specific to the heterodimerization partners.

Methods: a number of readouts can be used to assess the efficacy, and specificity, of ErbB2 compounds/antibodies in cell-based assays of ligand-induced heterodimer formation. Activity can be assessed by one or more of the following:

(i) Inhibition of ligand-induced heterodimerisation of ErbB2 with other ErbB family members in a target cell line, for example MCF-7 breast cancer cells. Immunoprecipitation of ErbB2 complexes from cell lysates can be performed with a receptor-specific antibody, and the absence/presence of other ErbB receptors and their biologically relevant ligands within the complex can be analysed following electrophoresis/Western transfer by probing with antibodies to other ErbB receptors.

(ii) Inhibition of the activation of signalling pathways by ligand-activated heterodimers. Association with ErbB2 appears critical for other members of the ErbB

family of receptors to elicit maximal cellular response following ligand binding. In the case of the kinase-defective ErbB3, ErbB2 provides a functional tyrosine kinase domain to enable signalling to occur following binding of growth factor ligands. Thus, cells co-expressing ErbB2 and ErbB3 can be treated with ligand, for example heregulin, in the absence and presence of inhibitor and the effect on ErbB3 tyrosine phosphorylation monitored by a number of ways including immunoprecipitation of ErbB3 from treated cell lysates and subsequent Western blotting using anti-phosphotyrosine antibodies (see Agus op. cit. for details). Alternatively, a high-throughput assay can be developed by trapping ErbB3 from solubilized lysates onto the wells of a 96-well plate coated with an anti-ErbB3 receptor antibody, and the level of tyrosine phosphorylation measured using, for example, europium-labelled anti-phosphotyrosine antibodies, as embodied by Waddleton, D. et.al. Anal. Biochem. 309:150-157, 2002.

In a broader extension of this approach, effector molecules known to be activated downstream of activated receptor heterodimers, such as mitogen-activated protein kinases (MAPK) and Akt, may be analysed directly, by immunoprecipitation from treated lysates and blotting with antibodies that detect the activated forms of these proteins, or by analysing the ability of these proteins to modify/activate specific substrates.

(iii) Inhibition of ligand-induced cellular proliferation. A variety of cell lines are known to co-express combinations of ErbB receptors, for example many breast and prostate cancer cell lines. Assays may be performed in 24/48/96-well formats with the readout based around DNA synthesis (tritiated thymidine incorporation), increase in cell number (crystal violet staining) etc. However, co-expression of ErbB1 or ErbB4 in such cell lines will mean that it is difficult to determine whether ErbB1 or ErbB4 homodimer signalling is responsible for the proliferative response to ligand.

A new, semi-automated assay system to monitor ErbB2 signalling activity that may be used to confirm the ability of candidate compounds to interact with and modulate ErbB2 activity has been developed. This assay exploits the heterodimerization characteristic of the ErbB family of receptor. We have created a BaF/3 cell line, which normally does not express any members of the ErbB family and is IL-3 dependent, that co-expresses wild-type ErbB2 and a kinase defective (but ligand responsive) ErbB-1 mutant (EGFR-K721R). Upon exposure of the cells to EGF (or other ErbB1 ligand),

heterodimer formation occurs leading to phosphorylation of the kinase-defective ErbB1 by the ErbB2 kinase, initiation of the signal transduction pathways downstream of the receptors and ultimately to DNA synthesis. In this experimental system signalling is strictly ligand-dependent but is entirely mediated by the ErbB2 kinase, providing a specific and sensitive assay for inhibitors of ErbB2 heterodimerization. Non-specific toxicity of the test samples is assessed in parallel by testing the cells' responsiveness to IL-3 in the absence of EGF.

Method: BaF/3 cells co-expressing EGFR-K721R and full length wild type ErbB2 are routinely grown in RPMI/10%FCS containing IL-3. Before assay, cells are washed three times to remove residual IL-3 and resuspended in RPMI 1640 + 10% FCS. Cells are seeded into 96 well plates using a Biomek 2000 (Beckman) at $2x10^4$ cells per 200µl and incubated for 4 hours at 37°C in 10% CO_2. Putative ErbB2 inhibitors are added to the first titration point and titrated in two-fold dilutions across the 96 well plate in duplicate with or without a constant amount of EGF (1nM) or IL-3 (1µl). ^{3}H-Thymidine (0.5µCi/well) is added and the plates incubated for 20 hours at 37°C in 5% CO_2. At the end of the incubation the cells are lysed in 0.5M NaOH at room temperature for 30 minutes then harvested onto nitrocellulose filter mats using an automatic harvester (Tomtec, Connecticut, USA). The mats are dried, placed in a plastic counting bag and scintillant (10ml) added. Incorporated 3H-Thymidine is determined using a beta counter (1205 Betaplate, Wallac, Finland).

(iv) Inhibition of growth in soft-agar. This is the benchmark-type assay undertaken to assess anti-tumour activity prior to xenograft studies in animals. Cells are seeded into liquid soft agar cultures, the agar allowed to set, and the appearance of cell colonies monitored over the next 14-21 days. The appearance of colonies in semi-solid media is known as anchorage-independent growth, and is characteristic of the tumour phenotype. Cultures of tumour cell lines can be set up in the presence of both ligand and candidate antagonists of receptor heterodimerisation, and colony growth monitored.

(v) Ability of candidate compounds to block *in vivo* growth of tumour xenografts of human tumour cell lines whose tumorigenic phenotype is known to be at least partly dependent on ligand activation of ErbB2 heterodimer cell signalling e.g. MCF7 breast cancer cells, LNCap prostate cancer cells etc. This can be assessed in

immunocompromised mice either alone or in combination with an appropriate cytotoxic agent for the cell line in question.

Modulation of ligand-receptor interaction

Rationale & method: ErbB2 has no identified ligand of its own, yet in association with other ErbB family members can markedly influence the interaction of its heterodimer partner with ligand.

(i) Heterodimers of ErbB2/3, either on the cell-surface or generated as recombinant fusion proteins using an immunoglobulin Fc domain, bind heregulin with 2-3 orders of magnitude higher affinity than the equivalent ErbB3 homodimers (Jones, J.T. et. al. FEBS Lett. 447:227-231, 1999). Similarly, ErbB4 homodimers do not bind EGF, whereas ErbB2/4 heterodimers do (Jones op.cit.). The heterodimer antagonist antibody 2C4 blocks heregulin binding to cell-surface and Fc fusion heterodimers very efficiently, possibly as a result of steric hindrance through the ligand-binding site, although this remains to be established. This observation suggests that candidate inhibitors of heterodimer association, in particular the ErbB2 CR1 loop-specific antibodies can be tested for activity in this manner. Hence, it is possible to assay in a 96-well format the ability of lead entities (which may or may not be antibodies) to block the binding of tagged ligand, for example europium-labelled EGF, to immobilised ErbB2 hetrodimer combinations, in one example ErbB2/4 Fc fusion proteins, using time-resolved fluorescence as a readout.

(ii) Berezov, A. et. al. J. Biol. Chem. 277: 28330-28339 (2002) describe a screen using the BIAcore whereby small ErbB2 peptide mimetics are used to inhibit heterodimer formation between immobilised ErbB1, 2 or 3 ectodomains and a solution containing ErbB3 ectodomain and ligand (heregulin). The peptides are derived from the C-terminal region of the second cysteine-rich domain of ErbB2.

Molecular replacement/binding

The structure coordinates of ErbB2, such as those set forth in Appendix I, can also be used for determining at least a portion of the three-dimensional structure of a molecular complex which contains at least some structural features similar to at least a portion of ErbB2. In particular, structural information about another crystallised molecular

complex may be obtained. This may be achieved by any of a number of well-known techniques, including molecular replacement.

Methods of molecular replacement are generally known by those of skill in the art (generally described in Brunger, Meth. Enzym., vol. 276, pp. 558-580, 1997; Navaza and Saludjian, Meth. Enzym., vol. 276, pp. 581-594, 1997; Tong and Rossmann, Meth. Enzym., vol. 276, pp. 594-611, 1997; Bentley, Meth. Enzym., vol. 276, pp. 611-619, 1997); Lattman, "Use of the Rotation and Translation Functions", in Meth. Enzymol., 115, pp. 55-77 (1985); and Rossmann, ed., "The Molecular Replacement Method", Int. Sci. Rev. Ser., No. 13, Gordon & Breach, New York (1972)).

Generally, X-ray diffraction data are collected from the crystal of a crystallised target structure. The X-ray diffraction data is transformed to calculate a Patterson function. The Patterson function of the crystallised target structure is compared with a Patterson function calculated from a known structure (referred to herein as a search structure). The Patterson function of the crystallised target structure is rotated on the search structure Patterson function to determine the correct orientation of the crystallised target structure in the crystal. The translation function is then calculated to determine the location of the target structure with respect to the crystal axes. Once the crystallised target structure has been correctly positioned in the unit cell, initial phases for the experimental data can be calculated. These phases are necessary for calculation of an electron density map from which structural differences can be observed and for refinement of the structure. Preferably, the structural features (e.g., amino acid sequence, conserved di-sulphide bonds, and beta-strands or beta-sheets) of the search molecule are related to the crystallised target structure.

The electron density map can, in turn, be subjected to any well-known model building and structure refinement techniques to provide a final, accurate structure of the unknown crystallised molecular complex (eg see Jones, T.A., Zou, J.Y., Cowan, S.W., and Kjeldgaard (1991). Improved methods for binding protein models in electron density maps and the location of errors in these models. Acta Crystallogr. A 47,110–119; Brunger, A.T., Adams, P.D., Clore, G.M., DeLano, W.L., Gros, P., Grosse-Kunstleve, R.W., Jiang, J.S., Kuszewski, J., Nilges, M., Pannu, N.S., et al. (1998). Crystallography and NMR system: a new software suite for macromolecular structure determination. Acta Crystallogr. D Biol. Crystallogr. 54, 905–921).

Obtaining accurate values for the phases, by methods other than molecular replacement, is a time-consuming process that involves iterative cycles of approximations and refinements and greatly hinders the solution of crystal structures. However, when the crystal structure of a protein containing at least a homologous portion has been solved, the phases from the known structure provide a satisfactory estimate of the phases for the unknown structure.

By using molecular replacement, all or part of the structure coordinates of ErbB2 provided herein (and set forth in Appendix) can be used to determine the structure of a crystallised molecular complex whose structure is unknown more rapidly and efficiently than attempting to determine such information ab initio. This method is especially useful in determining the structure of ErbB2 mutants and homologues.

The structure of any portion of any crystallised molecular complex that is sufficiently homologous to any portion of the extracellular domain of ErbB2 can be solved by this method.

Such structure coordinates are also particularly useful to solve the structure of crystals of ErbB2 co-complexed with a variety of molecules, such as other EGF receptor family receptors to which ErbB2 dimerises, or chemical entities. For example, this approach enables the determination of the optimal sites for the interaction between chemical entities, and the interaction of candidate ErbB2 agonists or antagonists.

All of the complexes referred to above may be studied using well-known X-ray diffraction techniques and may be refined versus 1.5-3.5 A resolution X-ray data to an R value of about 0.25 or less using computer software, such as X-PLOR (Yale University, distributed by Molecular Simulations, Inc.; see Blundell & Johnson, supra; Meth. Enzymol., vol. 114 & 115, H. W. Wyckoff et al., eds., Academic Press (1985)). This information may thus be used to optimize known ErbB2 agonist/antagonists, such as anti-ErbB2 antibodies, and more importantly, to design new or improved ErbB2 agonists/antagonists.

Production of ErbB2 crystals

The crystals of the present invention may be prepared by expressing a nucleotide sequence encoding ErbB2 or a variant thereof in a suitable host cell, and then

crystallising the purified protein(s). Preferably the ErbB2 polypeptide contains the extracellular domain (amino acids 1 to 632 of the mature human polypeptide or a truncated version thereof, preferably comprising amino acids 1 to 509, or the equivalent residues in other ErbB2 polypeptides) but lacks the transmembrane and intracellular domains. Preferred host cells are those that provide for reduced glycosylation of recombinant polypeptides, such as a glycosylation-defective mammalian cell line e.g. the Lec8 Chinese hamster cell line, a derivative of CHO-K1 fibroblasts (ATCC CRC:1737) (Stanley, 1989, Mol. Cell Biol. 9: 377-383).

ErbB2 polypeptides may also be produced as fusion proteins, for example to aid in extraction and purification. Examples of fusion protein partners include glutathione-S-transferase (GST), hexahistidine, GAL4 (DNA binding and/or transcriptional activation domains) and beta-galactosidase. It may also be convenient to include a proteolytic cleavage site between the fusion protein partner and the protein sequence of interest to allow removal of fusion protein sequences.

After expression, the proteins may be purified and/or concentrated, for example by immobilised metal affinity chromatography, ion-exchange chromatography, and/or gel filtration.

The protein(s) may be crystallised using known techniques. Usually, in a crystallisation process, a crystallisation buffer is prepared with a lower concentration of a precipitating agent necessary for crystal formation. For crystal formation, the concentration of the precipitating agent has to be increased, by addition of precipitating agent or by diffusion of the precipitating agent between the crystallisation buffer and a reservoir buffer. Diffusion may be achieved by known techniques such as the "hanging drop" or the "sitting drop" method. In these methods, a drop of crystallisation buffer containing the protein (s) is hanging above or sitting beside a much larger pool of reservoir buffer. Alternatively, the balancing of the precipitating agent can be achieved through a semi-permeable membrane that separates the crystallisation buffer and prevents dilution of the protein into the reservoir buffer.

We have found that the inclusion of about 15% PEG 1500 provides optimal crystallization conditions for the extracellular domain of human ErbB2.

Generating the crystal structure

Once the crystals have been obtained, the structure may be solved by known X-ray diffraction techniques. Many techniques use chemically modified crystals, such as those modified by heavy atom derivatization. In practice, a crystal is soaked in a solution containing heavy metal atom salts, or organometallic compounds, e. g., lead chloride, gold thiomalate, thimerosal or uranyl acetate, which can diffuse through the crystal and bind to the surface of the protein. The location(s) of the bound heavy metal atom(s) can then be determined by X-ray diffraction analysis of the soaked crystal. The patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centres) of the crystal can be solved by mathematical equations to give mathematical coordinates. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. The electron density maps are used to establish the positions of the individual atoms within the unit cell of the crystal (Blundel, T. L. and N. L. Johnson, Protein Crystallography, Academic Press (1976)).

Target binding sites for modulators of ErbB2

The three-dimensional structure of ErbB2 provided herein allows the identification of target binding sites for potential ErbB2 modulators.

Preferred target binding sites are those involved in heterodimerisation of ErbB2 with other members of the EGF receptor family, such as ErbB1, ErbB3 and/or ErbB4.

One preferred binding site involved in heterodimerisation is the CR1 dimerisation loop (residues 247-268) and adjacent residues (residues 244-246, 285-289). Other suitable binding sites include the N-terminal end of the CR1 domain (residues 200-203, 210-213, 216-218, 225-230), and the C-terminal end of the CR1 domain (residues 294-319).

In a further preferred embodiment, the binding site is the docking site on ErbB2 for the CR1 dimerisation loop of heterodimer partners. This docking site is located on ErbB2 between the L1, CR1 and L2 domains. Preferably, the docking site comprises the following ErbB2 residues: Gln 36, Gln 60, Arg 82, Thr 84, Gln 85, Phe 237, Thr 269, Phe 270, Gly 271, Ala 272, Tyr 282, Thr 285, Gly 288, Ser 289, Cys 290, Thr 291, Leu 292, Val 293, Cys 294, Pro 295 and Cys 310.

In yet another preferred embodiment, the target binding site is located on the L1 or L2 domains. Unlike the unligated structure of ErbB3 (Cho, H. S. & Leahy, D. J. Science 297, 1330–1333 (2002)) or the pseudo-unligated structure of EGFR (Ferguson et al., Molecular Cell, Vol. 11, 507–517, (2003)), the structure of ErbB2 exists in a conformation similar to that of the 2:2 ligand-receptor dimer. This is in large part maintained by the L1:L2 contact, as described in Garrett, et al., Molecular Cell, Vol. 11, 495-505. Thus a small molecule or antibody which binds to either the L1 or L2 domain or intercalates between them can modulate receptor dimer formation by either preventing the domains from binding to each other or by modifying the relative positions of the domains. Thus binding of a chemical entity to the L1 and/or L2 domain may cause the protein to adopt a conformation similar to that of its unligated relatives (EGFR or ErbB3) and thereby inhibit dimerisation. Alternatively, binding of a chemical entity to the L1 and/or L2 domain may cause modifications in the CR1 (dimerisation domain) as described in Garrett, et al., Molecular Cell, Vol. 11, 495-505 to inhibit receptor dimer formation. The relevant binding sites of the L1 or L2 domain consist of the atoms of either one of these domains that lie within about 4.5 Angstroms of the other domain.

Antibodies

The term "antibody" as used in this invention includes intact molecules as well as fragments thereof, such as Fab, F(ab')2, and Fv which are capable of binding the epitopic determinant. These antibody fragments retain some ability to selectively bind with its antigen or receptor and are defined as follows:

(1) Fab, the fragment which contains a monovalent antigen-binding fragment of an antibody molecule can be produced by digestion of whole antibody with the enzyme papain to yield an intact light chain and a portion of one heavy chain;

(2) Fab', the fragment of an antibody molecule can be obtained by treating whole antibody with pepsin, followed by reduction, to yield an intact light chain and a portion of the heavy chain; two Fab' fragments are obtained per antibody molecule;

(3) (Fab')2, the fragment of the antibody that can be obtained by treating whole antibody with the enzyme pepsin without subsequent reduction; F(ab)2 is a dimer of two Fab' fragments held together by two disulfide bonds;

(4) Fv, defined as a genetically engineered fragment containing the variable region of the light chain and the variable region of the heavy chain expressed as two chains; and

(5) Single chain antibody ("SCA"), defined as a genetically engineered molecule containing the variable region of the light chain, the variable region of the heavy chain, linked by a suitable polypeptide linker as a genetically fused single chain molecule.

Methods of making these fragments are known in the art. (See for example, Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, New York (1988), incorporated herein by reference).

Antibodies of the present invention may be produced, for example, by immunizing mice with purified ErbB2 fragment 1-509. After determining that the mice are producing anti-ErbB2 antibodies, hybridomas may be prepared and antibody specificity assayed by ELISA or Flow Cytometry using two cell lines: Baf/wt-EGFR cells and Baf/EGFR-"mutation x" cells. These mouse cell lines express either the wild type ErbB2 or the ErbB2 containing an amino acid substitution, for example an Ala substitution (ie mutation x), within the specific site against which the antibody is to be directed. When hybridomas secreting antibodies which recognize Baf/wt-ErbB2, but not Baf/ErbB2-"mutant x" are identified, the corresponding hybridoma may be cloned and the monoclonal antibody purified.

Alternatively, in raising antibodies of the invention, it may be desirable to use derivatives of the peptides or loop structures which are conformationally constrained. Conformational constraint refers to the stability and preferred conformation of the three-dimensional shape assumed by a peptide. Conformational constraints include local constraints, involving restricting the conformational mobility of a single residue in a peptide; regional constraints, involving restricting the conformational mobility of a group of residues, which residues may form some secondary structural unit; and global constraints, involving the entire peptide structure. For example, amino acids adjacent to or flanking the ErbB2 loop structures may be included in the construct to maintain conformation of the peptide used to raise antibodies.

In addition, the active conformation of the peptide may be stabilized by a covalent modification, such as cyclization or by incorporation of gamma-lactam or other types of bridges. For example, side chains can be cyclized to the backbone so as create a L-gamma-lactam moiety on each side of the interaction site. See, generally, Hruby et al., "Applications of Synthetic Peptides," in Synthetic Peptides: A User's Guide: 259-345 (W. H. Freeman & Co. 1992). Cyclization also can be achieved, for example, by formation of cystine bridges, coupling of amino and carboxy terminal groups of respective terminal amino acids, or coupling of the amino group of a Lys residue or a related homolog with a carboxy group of Asp, Glu or a related homolog. Coupling of the alpha-amino group of a polypeptide with the epsilon-amino group of a lysine residue, using iodoacetic anhydride, can be also undertaken. See Wood and Wetzel, 1992, Int'l J. Peptide Protein Res. 39: 533-39.

Further the conformation of the peptide analogues may be stabilised by including amino acids modified at the alpha carbon atom (eg. α-amino-150-butyric acid) (Burgess and Leach, 1973, Biopolymers 12(12):2691-2712; Burgess and Leach, 1973, Biopolymers 12(11):2599-2605) or amino acids which lead to modifications on the peptide nitrogen atom (eg. sarcosine or N-methylalanine) (O'Donohue et al, 1995, Protein Sci. 4(10):2191-2202).

Another approach described in US 5,891,418 is to include a metal-ion complexing backbone in the peptide structure. Typically, the preferred metal-peptide backbone is based on the requisite number of particular coordinating groups required by the coordination sphere of a given complexing metal ion. In general, most of the metal ions that may prove useful have a coordination number of four to six. The nature of the coordinating groups in the peptide chain includes nitrogen atoms with amine, amide, imidazole, or guanidino functionalities; sulfur atoms of thiols or disulfides; and oxygen atoms of hydroxy, phenolic, carbonyl, or carboxyl functionalities. In addition, the peptide chain or individual amino acids can be chemically altered to include a coordinating group, such as for example oxime, hydrazino, sulfhydryl, phosphate, cyano, pyridino, piperidino, or morpholino. The peptide construct can be either linear or cyclic, however a linear construct is typically preferred.

Peptides and Peptidomimetics

In yet a further aspect the present invention provides an isolated conformationally constrained peptide or peptidomimetic consisting essentially of (i) ErbB2 amino acid residues 200-203, (ii) ErbB2 amino acid residues 210-213, (iii) ErbB2 amino acid residues 216-218, (iv) ErbB2 amino acid residues 225-230, (v) ErbB2 amino acid residues 247-268 or a subset thereof; (vi) ErbB2 amino acid residues 244-246, (vii) ErbB2 amino acid residues 285-289, or (viii) ErbB2 amino acid residues 294-319 or a subset thereof.

The term "conformationally constrained molecules" means conformationally constrained peptides and conformationally constrained peptide analogues and derivatives.

The term "analogues" refers to molecules having a chemically analogous structure to the naturally occurring alpha-amino acids present in ErbB2. Examples include molecules containing *gem*-diaminoalkyl groups or alklylmalonyl groups.

The term "derivatives" includes alpha amino acids wherein one or more side groups found in the naturally occurring alpha-amino acids present in ErbB2 have been modified. Thus, for example the naturally-occurring amino acids present in ErbB2 may be replaced with a variety of uncoded or modified amino acids such as the corresponding D-amino acid or N-methyl amino acid. Other modifications include substitution of hydroxyl, thiol, amino and carboxyl functional groups with chemically similar groups.

The present invention encompasses the use of conformationally constrained peptidomimetics of fragments of ErbB2 (such as amino acid residues 247-268), i.e. analogues and derivatives which mimic the activity of ErbB2 and are therefore capable of modulating ErbB2 activity *in vivo*. These peptidomimetics are preferably substantially similar in three-dimensional shape to the peptide structures (for example, loop structures) as they exist on the native ErbB2. Substantial similarity means that the geometric relationship of groups in the ErbB2 peptide fragment is preserved such that the peptidomimetic will mimic the activity of ErbB2 *in vivo*.

A "peptidomimetic" is a molecule that mimics the biological activity of a peptide but is no longer peptidic in chemical nature. By strict definition, a peptidomimetic is a molecule that no longer contains any peptide bonds (that is, amide bonds between amino acids). However, the term peptide mimetic is sometimes used to describe molecules that are no longer completely peptidic in nature, such as pseudo-peptides, semi-peptides and peptoids. Whether completely or partially non-peptide, peptidomimetics for use in the methods of the invention provide a spatial arrangement of reactive chemical moieties that closely resembles the three-dimensional arrangement of active groups in the peptide on which the peptidomimetic is based. As a result of this similar active-site geometry, the peptidomimetic has effects on biological systems which are similar to the biological activity of the peptide.

There are clear advantages for using a mimetic of a given peptide rather than the peptide itself, because peptides commonly exhibit two undesirable properties: (1) poor bioavailability; and (2) short duration of action. Peptide mimetics offer an obvious route around these two major obstacles, since the molecules concerned are small enough to be both orally active and have a long duration of action. There are also considerable cost savings and improved patient compliance associated with peptide mimetics, since they can be administered orally compared with parenteral administration for peptides. Furthermore, peptide mimetics are much cheaper to produce than peptides.

Suitable peptidomimetics based on, for example, residues 247-268, can be developed using readily available techniques. Thus, for example, peptide bonds can be replaced by non-peptide bonds that allow the peptidomimetic to adopt a similar structure, and therefore biological activity, to the original peptide. Further modifications can also be made by replacing chemical groups of the amino acids with other chemical groups of similar structure. The development of peptidomimetics derived from ErbB2 peptides based on residues 247-268 can be aided by reference to the three dimensional structure of these residues as provided in Appendix I. This structural information can be used to search three-dimensional databases to identify molecules having a similar structure, using programs such as MACCS-3D and ISIS/3D (Molecular Design Ltd., San Leandro, CA), ChemDBS-3D (Chemical Design Ltd., Oxford, U.K.), and Sybyl/3DB Unity (Tripos Associates, St. Louis, MO).

Those skilled in the art will recognize that the design of a peptidomimetic may require slight structural alteration or adjustment of a chemical structure designed or identified using the methods of the invention. In general, chemical compounds identified or designed using the methods of the invention can be synthesized chemically and then tested for ability to modulate ErbB2 activity using any of the methods described herein. The methods of the invention are particularly useful because they can be used to greatly decrease the number potential mimetics which must be screened ability to modulate ErbB2 activity.

The peptides or peptidomimetics of the present invention can be used in assays to screening for candidate compounds which bind to regions of ErbB2 and potentially interfere with the hereodimerisation of ErbB2 with another member of the EGF receptor family.

Standard solid-phase ELISA assay formats are particularly useful for identifying inhibitors of dimerisation. In accordance with this embodiment, the peptide or peptidomimetic of the invention is immobilized on a solid matrix, such as, for example an array of polymeric pins or a glass support. Conveniently, the immobilized peptide or peptidomimetic is a fusion polypeptide comprising Glutathione-S-transferase (GST; e.g. a CAP-ERK fusion), wherein the GST moiety facilitates immobilization of the protein to the solid phase support. This assay format can then be used to screen for candidate compounds that bind to the immobilised peptide or peptidomimetic and/or interefere with binding of a natural binding partner of ErbB2 to the immobilised peptide or peptidomimetic.

Uses of modulators of ErbB2

Compounds/chemical entities designed or selected by the methods of the invention described above may be used to modulate ErbB2 activity in cells, i.e. activate or inhibit ErbB2 activity. In particular, they may be used to modulate the interaction between ErbB2 and other heterodimerisation partners of the EGF receptor family, such as ErbB1, ErbB2 and ErbB4.

Modulation of heterodimerisation between ErbB2 and other members of the EGF receptor family may be achieved by direct binding of the chemical entity to a

heterodimerisation surface of ErbB2 and/or by an allosteric interaction elsewhere in the ErbB2 extracellular domain.

Given that aberrant EGF/ErbB2 activity is implicated in a range of disorders, the compounds described above may also be used to treat, ameliorate or prevent disorders characterised by abnormal ErbB2 signalling. Examples of such disorders include malignant conditions including tumours of the brain, head and neck, prostate, ovary, breast, cervix, lung, pancreas and colon; and melanoma, rhabdomyosarcoma, mesothelioma, squamous carcinomas of the skin and glioblastoma.

Administration

Compounds of the invention, i.e. antibodies of the invention or modulators of ErbB2 identified or identifiable by the screening methods of the invention, may preferably be combined with various components to produce compositions of the invention. Preferably the compositions are combined with a pharmaceutically acceptable carrier or diluent to produce a pharmaceutical composition (which may be for human or animal use).

The formulation will depend upon the nature of the compound and the route of administration but typically they can be formulated for topical, parenteral, intramuscular, oral, intravenous, intra-peritoneal, intranasal inhalation, lung inhalation, intradermal or intra-articular administration. The compound may be used in an injectable form. It may therefore be mixed with any vehicle which is pharmaceutically acceptable for an injectable formulation, preferably for a direct injection at the site to be treated, although it may be administered systemically.

The pharmaceutically acceptable carrier or diluent may be, for example, sterile isotonic saline solutions, or other isotonic solutions such as phosphate-buffered saline. The compounds of the present invention may be admixed with any suitable binder(s), lubricant(s), suspending agent(s), coating agent(s), solubilising agent(s). It is also preferred to formulate the compound in an orally active form.

In general, a therapeutically effective daily oral or intravenous dose of the compounds of the invention, including compounds of the invention and their salts, is likely to range from 0.01 to 50 mg/kg body weight of the subject to be treated, preferably 0.1 to 20

mg/kg. The compounds of the invention and their salts may also be administered by intravenous infusion, at a dose which is likely to range from 0.001-10 mg/kg/hr.

Tablets or capsules of the compounds may be administered singly or two or more at a time, as appropriate. It is also possible to administer the compounds in sustained release formulations.

Typically, the physician will determine the actual dosage which will be most suitable for an individual patient and it will vary with the age, weight and response of the particular patient. The above dosages are exemplary of the average case. There can, of course, be individual instances where higher or lower dosage ranges are merited, and such are within the scope of this invention.

For some applications, preferably the compositions are administered orally in the form of tablets containing excipients such as starch or lactose, or in capsules or ovules either alone or in admixture with excipients, or in the form of elixirs, solutions or suspensions containing flavouring or colouring agents.

The compositions (as well as the compounds alone) can also be injected parenterally, for example intravenously, intramuscularly or subcutaneously. In this case, the compositions will comprise a suitable carrier or diluent.

For parenteral administration, the compositions are best used in the form of a sterile aqueous solution which may contain other substances, for example enough salts or monosaccharides to make the solution isotonic with blood.

For buccal or sublingual administration the compositions may be administered in the form of tablets or lozenges which can be formulated in a conventional manner.

For oral, parenteral, buccal and sublingual administration to subjects (such as patients), the daily dosage level of the compounds of the present invention and their pharmaceutically acceptable salts and solvates may typically be from 10 to 500 mg (in single or divided doses). Thus, and by way of example, tablets or capsules may contain from 5 to 100 mg of active compound for administration singly, or two or more at a time, as appropriate. As indicated above, the physician will determine the actual

dosage which will be most suitable for an individual patient and it will vary with the age, weight and response of the particular patient.

The routes of administration and dosages described are intended only as a guide since a skilled practitioner will be able to determine readily the optimum route of administration and dosage for any particular patient depending on, for example, the age, weight and condition of the patient.

The present invention will now be described further with reference to the following examples, which are illustrative only and non-limiting. The examples refer to the figures:

EXAMPLES

Experimental Procedures

Construction of the ErbB2-509 expression vector

An ErbB2 cDNA clone encompassing the entire coding region in the expression vector pRc/CMV (Invitrogen) was a gift from Dr. Rod Fiddes (AMBRI Pty.Ltd.). A Hind lll/EcoR l fragment spanning the 5'-non-coding region and nucleotides encoding amino acids 1-412 was isolated and cloned into pUC19 (Pharmacia). A 324 basepair EcoRl fragment incorporating amino acids 413-509 of ErbB2 and a C-terminal FLAG epitope (Brizzard et al., 1994, Biotechniques 16, 730-735) was generated by the polymerase chain reaction (PCR) using the primers 5'-CGGACAGCCTGCCTGACCTC-3' (upstream) and 5'-CCGGAATTCTAGACTACTTATCATCGTCATCTTTGTAATCGTTGACACA CTGGGTGGGC-3', and cloned into the EcoR 1 site of this plasmid. This plasmid was further modified by replacement of the 5' Hind III/BamH I of ErbB2 with a truncated Hind III/BamH I fragment, corresponding to nucleotides 171-1170 (GenBank accession number X03363), generated by PCR using the primers 5'-GGGGAAGCTTGCCACCATGGAGCTGGCGGCC-3' (upstream) and 5'-GCTGCACTTCTCACACCGCTG-3' (downstream). The fidelity of all amplification products was established by nucleotide sequencing. The modified ErbB2 cDNA insert was subsequently excised as a Hind III/Xba I fragment and cloned into the corresponding restriction sites of the mammalian expression vector pEE14 (Bebbington

and Hentschel, 1987, .In: DNA Cloning (Glover, D., ed.), Vol. III, pp.163-188, IRL Press, Oxford, U.K) to generate pESE.ErbB2-509.

Cell culture and transfection

The Lec8 Chinese hamster cell line, a derivative of CHO-K1 fibroblasts was obtained from the American Tissue Culture Collection (ATCC CRC:1737) and maintained in Glasgow's modified Eagle's medium (Life Technologies) supplemented with 10% fetal calf serum (FCS). Cells were transfected with pESE.ErbB2-509 that had been linearised by digestion with Fsp I, using FuGENE (Roche Molecular Biochemicals) according to the manufacturer's instructions. Stable transfectants were isolated by culturing cells in glutamine-free medium containing 10% dialysed FCS and 25 μM methionine sulfoximine. Supernatants were screened by dot-blotting onto nitrocellulose and probing with the anti-FLAG monoclonal antibody, M2 (Brizzard et al., 1994).

Protein Production and Purification

A positive polyclonal culture was used for scale-up protein production by growing the cells in roller bottles, during which time they were adapted to DMEM/F12 (JRH) media, supplemented with 10% dialysed FCS (Life Techologies) and 25uM methionine sulfoximine. After verifying the yield and quality of the ErbB2-509 fragment, four 500ml spinner flasks, each containing 10 g of FibraCell disks (New Brunswick Scientific), were inoculated with harvested cells from eight confluent roller bottles. Over a period of three weeks, spent media was collected daily from the spinner flasks and replaced with fresh media. Undialysed serum (CSL) was used instead of dialysed serum after day three. Approximately 30 litres of media harvest was collected over three weeks.

ErbB2-509 FLAG-tagged protein was purified by immunoaffinity chromatography over a 50 ml column of M2 anti-FLAG antibody covalently coupled to Mini Leak Low (Kem-En-Tek Denmark) as per manufacturer's instructions. Batches of four to six litres of culture media at 4 °C were passed over the column at 100 – 200 ml/h and washed with ~20 column volumes of 40 mM Tris-buffered saline at pH8 /0.02% sodium azide (TBSA). FLAG-tagged protein was eluted from the column after 90 min of recirculating 50 ml of a 0.25 mg/ml solution of the FLAG peptide DYKDDDDK in TBSA, followed by elution with three to four column volumes of 0.1 mg/ml FLAG

peptide in TBSA. The affinity column was regenerated with 0.1M sodium citrate pH 3 before re-equilibration at pH 8 with TBSA, ready for the next batch of harvest. Further purification was effected by passing a concentrated solution of the peptide-eluted product over a Superdex 200 column (Pharmacia 26/60) in TBSA at 5 ml/min. Greater than 90% of the 280nm-absorbing material eluted as a single symmetrical peak of apparent mass ~70 kDa , at a yield of 1-2mg/L of the spinner-flask harvest. The peak fraction was buffer-exchanged into 10 mM HEPES pH7.5 and concentrated to 8mg/ml.

Crystallization and Data Collection

Crystallization trials were performed with a factorial screen (Jancarik and Kim, 1991, J. Appl. Cryst. 24, 409-411) using the hanging drop method. Initially, rod-shaped crystals grew within 4 days, which diffracted to ~3.5 Å. However, after further crystallization trials the best conditions were 15% PEG 1500 and the resolution extended to 2.5 Å. Crystals (space group $P2_12_12_1$, a=75.96, b=82.24, c=110.06 Å) were cryo-cooled to –170 °C in 20% PEG, 20% glycerol. Diffraction data were recorded as 192 1° exposures on a Rigaku RAXIS IV area detector using RU-300 Rigaku generator equipped with elliptical glass capillary optics (AXCO). Data were integrated to 2.5 Å and scaled using the DENZO/SCALEPACK (mosaic spread 0.8°, R_{sym}=0.103, multiplicity 7.2, completeness 97.2%)

Structure Solution and Refinement

The structure was solved by molecular replacement with AMORE using data 10-4 Å resolution and two fragments of EGFR (residues 4-238 and 310-500) as search models. In both rotation and translation functions the highest peaks corresponded to the correct solution. By inspection of electron density maps (10-3.5 Å resolution) with O an initial model of ErbB2 was constructed from the structure of EGFR. This model consisted of 472 of 510 residues, including 91 side chains truncated from the EGFR equivalent. Structure refinement was performed with CNS (Brunger et al., 1998, Acta Crystallogr. D Biol Crystallogr. 54, 905-921). Initially, rigid body refinement with four groups (residues 1-194, 197-310, 318-510) gave R=0.473, R_{free}=0.482 (5% of the data). Nine rounds of manual refitting were alternated with energy minimisation, B factor refinement and, sometimes, simulated annealing. The resolution was extended in a stepwise manner with a bulk solvent correction applied from round 3 and an overall anisotropic thermal parameter from round 6. The final model contains 506 amino

acids, 4 carbohydrate residues and 134 solvent molecules, giving R=0.226, R_{free}=0.264 (data 25-2.5 Å). For residues 1-2, 100-102 and 107-113 294-318 the electron density is weak and there is no density for residues 103-106 or beyond residue 510.

Database Preparation

Databases were generated using information provided by the Supplier, or the NIH developmental therapeutics program. The NCI database was built from the October 2000 release, and the Tripos Leadquest database using the October 2001 release. SDF records were converted into 3-dimensional Sybyl mol2 files using the dbtranslate utility from UNITY environment in sybyl6.7, coordinates were generated using Concord 4.0.2 and the atom typing of resulting mol2 files corrected using our in house tool Mol-prepare. The resulting mol2 files were then protonated, assigned Gasteiger-Huckel charges and minimized (conjugate gradient for a maximum of 500 iterations) using Sybyl 6.7. Databases were then indexed for our database server program.

Assay for determining ErbB2 kinase activity

BaF/3 cells co-expressing K721R-ErbB1 and wtErbB2 are routinely grown in RPMI/10%FCS containing IL-3. Before assay, cells are washed three times to remove residual IL-3 and resuspended in RPMI 1640 + 10% FCS. Cells are seeded into 96 well plates using a Biomek 2000 (Beckman) at $2x10^4$ cells per 200µl and incubated for 4 hours at 37°C in 10% CO_2. Candidate ErbB2 inhibitors are added to the first titration point and titrated in two-fold dilutions across the 96 well plate in duplicate with or without a constant amount of mEGF (1nM) or IL-3 (1µl). ^{3H}-Thymidine (0.5µCi/well) is added and the plates incubated for 20 hours at 37°C in 5% CO_2. At the end of the incubation the cells are lysed in 0.5M NaOH at room temperature for 30 minutes then harvested onto nitrocellulose filter mats using an automatic harvester (Tomtec, Connecticut, USA). The mats are dried, placed in a plastic counting bag and scintillant (10ml) added. Incorporated 3H-Thymidine is determined using a beta counter (1205 Betaplate, Wallac, Finland).

Example 1: Description of structure

The ErbB2 fragment described here comprises the L1, CR1 and L2 domains plus the first module (residues 489-509) from the second cys-rich region CR2. The crystals contained only one molecule of the truncated ErbB2 ectodomain in the asymmetric unit and showed no evidence of dimers. ErbB2 (residues 1-509) adopts a compact bilobed structure reminiscent of the closed conformation of the EGFR ectodomain in its 2:2 complexes with TGFα (Garrett et al., 2002) or EGF (Ogiso et al., 2002, Cell 110, 775-787), but very different from the open conformations seen in the unliganded, full length ErbB3 ectodomain (Cho and Leahy, 2002) or the truncated L1/CR/L2 fragment of the closely related type 1 insulin-like growth factor receptor (Garrett et al., 1998, Nature 394, 395-399).

The main chain conformation of each L domain is similar to the corresponding domains of EGFR with the rmsd for the Cα atoms of L1 being 1.14-1.21 (for >91% of the Cα atoms) and for the Cα atoms of L2 being 0.97-1.05 Å (96%). In the ErbB2 L1 domain, the V-shaped region (residues 9-17), which forms a substantial part of the ligand-binding surface in EGFR, is maintained. However there is a small shift in the position of the N-terminal helix (residues 17-30) in ErbB2 and minor differences in residues equivalent to those in EGFR that make a main chain contact with TGFα (Garrett et al., 2002). The position of the large insertion (residues 101-109) specific to ErbB2 (Figure 1) is in the loop of EGFR (residues 101-106) in the fourth repeat at the corner of the second and third β-sheets of the L1 domain and is predominantly disordered in ErbB2. In the ErbB2 L2 main chain, small movements are seen in the two loops (residues 324-334 and 360-374) equivalent to those that bind ligand in EGFR (Garrett et al., 2002) and in the relative position of the single cys rich module (residues 489-509) that follows the L2 domain.

While the folds of the two L domains are similar in ErbB2 and the EGFR/TGFα complex (Garrett et al., 2002) the relative orientation of these two domains are quite different (Figures 3 and 4). This is due to differences in the CR1 domain and the CR1-L2 hinge of ErbB2 which direct the two L domains towards each other, where they make substantial contact (the total accessible surface area buried is 1264 $Å^2$ and shape complimentarily, S_o = 0.63). The overall movement of the ErbB2 L2 domain, with respect to L1, corresponds to a rotation of about 35 ° (A 37.4 °, B 31.8 °) around an axis parallel to strands of the L2 large β-sheet and a translation of 7 Å towards CR1 so that

in ErbB2 the bottom of the large sheet on L2 sits against the N-terminal end (residues 1-33) of L1. In this conformation an EGF-like ligand cannot bind to sites on either the L1 or L2 domains of ErbB2 (as seen for EGFR) since each site is occluded by the opposing L domain.

Finding ErbB2 in this "closed" form raises the question of whether this could occur in the unligated form of EGFR (or ErbB3/ErbB4). Structural superposition is not straightforward as there are main chain rearrangements in this region of ErbB2, namely a shift in the N-terminal helix of L1 by about 1.8 Å, possibly due to Leu22 of ErbB2 being replaced by an aromatic side chain in ErbB1 (F24), ErbB3 (Y27) and ErbB4 (Y24) (Figure 1). However, even when superimposing residues 9-17 and the helix separately then comparing with superpositions of L2, complementarity in these regions for other members of the family was not observed. In EGFR, Gln411 is equivalent to Ala419 of ErbB2 and the bulky Gln side chain could not be easily accommodated in the ErbB2 structure as it would sterically clash with Ser26 and Met30 (Met24 and Leu28 in ErbB2). This closed conformation would not pose a problem for ErbB3/ErbB4 where the residues corresponding to ErbB2 Ala419 are Gly residues (Figure 1). Asn12 in EGFR is a key residue for ligand binding and is strictly conserved in all the EGFR family except ErbB2. If the unliganded form of EGFR were to have the same conformation as ErbB2 then Asn12 (equivalent to Met10 in ErbB2) would sterically clash with His409 (Asn417 in ErbB2) and the side chains of Lys463 and Lys465 (equivalent to the hydrophobic residues Ala471 and Leu473 of ErbB2) on the last strand of the major β-sheet of L2, would overlap with Arg29 and Asp22, respectively. In addition to the steric clash, electrostatic repulsion may also be important as residues 29 and 463 are basic (Lys/Arg) in EGFR/ErbB3/Erb4 but are His and Ala in ErbB2, respectively. Thus it appears that the "closed" conformation seen for domains 1-3 of ErbB2 is unlikely to be a general feature of this receptor family but unique to the ErbB2 molecule.

Example 2: Analysis of the ligand binding region

A comparison of the ErbB2 and EGFR structures shows why ErbB2 does not bind ligands such as EGF, TGFα or the neuregulins. The L domains of EGFR, together with the ligand, TGFα, were superimposed on the corresponding L domains of ErbB2 using the strands of the large β-sheet. Residues of ErbB2 L1 which would interfere with ligand binding are Arg13 (replacing Thr, Ser and Ser in ErbB1, ErbB3 and ErbB4) and

Pro15 (replacing Leu, Thr and Leu in ErbB1, ErbB3 and ErbB4) on the short N-terminal strand of the L1 domain (Figure 1). In EGFR, residues 13-15 form a β-sheet with the ligand. The presence of Arg13 alone is likely to prevent ligand binding as this residue lies at the heart of the interface. Unless the receptor side chains are small there is no room for ligand side chains. Another crucial residue in EGFR is Asn12, the side chain of which makes two hydrogen bonds to the ligand's main chain. Asn is present in EGFR, ErbB3 and ErbB4 but in ErbB2 the equivalent residue (Met10) is buried between Val8 and Pro15 and unavailable for ligand interactions. Another residue in the L1 domain which would interfere with EGF-related ligand binding by ErbB2 is Asp98, which is Ser or Leu in the other ErbB family members (Figure 1) and would clash with Glu27 of TGFα

Observations by Kohda et al., 1993 (J. Biol. Chem. 268, 1976-1981) indicate that ligands can bind to L2 alone albeit with low affinity. For the L2 domain the differences between ErbB2 and the other ErbB receptors are more subtle. Asp355 of EGFR, which makes a salt bridge with the highly conserved Arg42 of TGFα (Garrett et al., 2002), is conserved for all EGFR homologues including ErbB2. However, in ErbB2 movement of residues 324-334 in a neighbouring loop appears to disturb the position of this residue (Asp363). Other residues in the L2 binding site of EGFR such as His346 and Gln384 are smaller in ErbB2 (Ala354 and Ser392), so binding to ErbB2 would be expected to be of lower affinity.

The ligand-binding surfaces of the EGFR homologues are by no means well conserved and each ErbB receptor has its own ligand binding characteristics. ErbB3 and ErbB4 predominantly bind the neuregulin group. Again, ErbB2 fails to interact with this subfamily of ligands and the residues of ErbB2 at positions equivalent to the EGFR ligand binding surface clearly disrupt the L1 and L2 binding surface (Figure 1).

Example 3: Differences in CR1

In the TGFα:EGFR complex, the dominant feature of CR1 is a large loop (residues 242-259) which extends out from the rod-shaped CR1 and plays a key role in homo-dimerisation and signaling for that receptor. This loop contains only limited sequence homology with the other EGFR homologues (33-44%) and it was not clear whether dimerisation of the receptor influenced the conformation of this loop. In the crystal, ErbB2 is present as a monomer and the CR1 loop projects out into solvent, lying

against an adjacent molecule in a crystal contact. Superposition of this loop from ErbB2 and EGFR shows that the main chain of the ErbB2 loop adopts a very similar structure to that found in the EGFR dimer (rmsd 0.61 A for 15 Cα's) with small differences seen only at the tip. Thus it seems that this loop has a well defined conformation even in the undimerised state. Residues important in maintaining this structure are prolines found at various positions in different homologues, particularly Pro257 (EGFR), and two completely conserved asparagines (residues 247 and 256 in EGFR) which make hydrogen-bonded contacts with main chain atoms. In ErbB2 this loop is bent slightly (12-13°) relative to the corresponding fifth cys rich module in EGFR.

Overall comparison of the CR1 domain shows that, relative to EGFR, it does not bend smoothly, rather it bends locally at three places. For individual modules rms deviations in Cα positions are less than 1 Å while for the whole domain the rms deviation is 1.7/1.8 Å (106/98 of 117 residues). Cys rich modules 2-4 lie similarly against L1 in both ErbB2 and EGFR and the bends occur at the interfaces of the fourth and seventh modules. The most obvious bend is in the middle of CR1 between the fourth and fifth modules (21/25°) but other differences (between the fifth and sixth modules 11°, between the sixth and seventh modules 15/27°), together with a bend of 37/32° between the seventh module and the L2 domain constitute the set of changes which reorientate L2 with respect to L1.

Example 4: Implications for dimerisation

The rearrangements in CR1 have three effects on the dimer interface as seen in EGFR and the capacity of ErbB2, in this conformation, to form heterodimers with a 1:1 complex of EGFR with ligand. Superposing the fifth cys-rich module from CR1 of ErbB2 on one half of the EGFR dimer, the bend at the fourth and fifth modules of ErbB2 causes the N-terminal tip of ErbB2 to move away from the corresponding region on the other molecule, removing that region from the back-to-back contact. The bend at cys-rich modules 6 and 7 of ErbB2 would bring module 8 in contact with module 7 of EGFR. More significant, however, is that the bend at the fourth and fifth modules of ErbB2 brings the ErbB2 L1domain closer to the tip of the partner's CR1 loop, causing Thr249 of EGFR) to overlap with Thr84 and Gln60 of ErbB2. Therefore it seems unlikely that ErbB2 could interact with EGFR in the closed form. With some minor

structural rearrangement the tip of ErbB2's CR1 loop could be accommodated in EGFR.

Example 5: *In silico* screening for compounds that modulate ErbB2 activity

Molecular docking of large compound data bases to target proteins of known or modeled 3-dimensional structure is now a common approach in the identification of new lead compounds. This "virtual screening" approach relies on fast and accurate estimation of the ligand binding mode and an estimate of ligand affinity. Typically a large database of compounds, either real or virtual is docked to a target structure and a list of the best potential ligands is produced. This ranking should be highly enriched for active compounds which may then be subject to further experimental validation.

The calculation of the ligand binding mode may carried out by molecular docking programs which are able to dock the ligands in a flexible manner to a static protein structure. The estimation of ligand affinity is typically carried out by the use of a separate scoring function. These scoring functions include empirical functions [DOCK potential energy, Chemscore, Score], or knowledge based potentials of mean force [PMF, SMoG]. Consensus scoring involves re-scoring each ligand with multiple scoring functions and then using a combination of these rankings to generate a hit list.

We used the program DOCK (vers. 4.0.1) for the generation of favorable conformations of ligand binding. Protons and Kollman all-atom charges were added to the protein using the Biopolymer module of Sybyl6.7 and proton positions minimized with all other atoms held fixed. Scoring grids were calculated using the GRID program with a grid resolution of 0.25 Angstrom. All conformations were minimized using the DOCK energy function. Docking of ligand databases were directed towards the sites identified previously. Nine scoring functions were used, including Score, the Score-Quality estimate, DOCK energy function, PMF, PMF-RB (the PMF function with penalties for rotatable bonds), the SMoG function, SMoG/H (the SMOG function scaled by the number of ligand heavy atoms), Chemscore, and the Autodock Scoring function. Ligand conformations were chosen using a rank-by-rank consensus of the nine different scoring methods of the best 25 solutions obtained from the DOCK program using the DOCK potential energy. A ranked list of compounds was generated using a consensus of the individual scores for each ligand (in their best consensus-ranked conformation).

Four of the top-ranked compounds (compounds 39293, 94289, 19378 and 20697) were obtained and tested for their ability to modulate ErbB2 kinase activity according to the method described above. The results of these inhibition assays are shown in Figure 3. These results show that all four compounds tested inhibited ErbB2 kinase activity at concentrations of between 10^{-1} and 10^{2} μM.

Conclusion

The availability of 3D structures for the ErbB2(1-509) monomer, the 2:2 dimer complexes of TGFα:sEGFR501 (Garrett et al., 2002) and EGF:EGFR621 (Ogiso et al., 2002), the unliganded ErbB3 ectodomain monomer (Cho and Leahy, 2002) and the related L1/cys-rich/L2 fragment of the IGF-1R (Garrett et al., 1998) provides the framework to explore some of the outstanding issues related to ErbB receptor function. A striking feature in these comparisons is the flexibility that exists at the CR1/L2 junction resulting in major differences in the positioning of the L2 domain relative to the L1/CR1 region.

The structure of the unliganded ErbB3 full length ectodomain is even more open than that of the IGF-1R fragment, with the L2 domain rotated further away from the L1 domain (Figure 3). This open conformation is very different from the closed arrangement of the L1 and L2 domains seen in the two EGFR/ligand dimer structures and in the ErbB2(1-509) structure reported here. The open conformation is stabilised by a single main chain/main chain hydrogen bond and side chain interactions between residues Tyr246, Phe251 and Gln252 in the CR1 loop (residues 242-259) and Asp562, Gly563, His565 (module 5) and Lys583 (module 6) of CR2. These contact residues are conserved in EGFR and ErbB4 but not in ErbB2 (Cho and Leahy, 2002). This open structure of ErbB3 provides an explanation for the predominantly low affinity ligand binding by soluble full length EGFR ectodomain compared to the high affinity binding shown by sEGFR501, which cannot make these contacts since it lacks CR2 modules 2 to 7. The same CR1 loop is critically involved in formation of the ligand-induced EGFR dimers suggesting that it becomes available for such dimer interactions following ligand binding.

The "closed" structure of the unliganded ErbB2(1-509) fragment seen here, where the bottom of the L2 domain sits against the top of the L1 domain resembles a "pseudo-

active" arrangement of domains, similar to that seen in the EGFR/ligand complexes (Garrett et al., 2002; Ogiso et al., 2002). It may represent the conformation of the full length ectodomain, since the residues involved in the ErbB3 CR1 loop/CR2 interactions are not conserved in ErbB2 (Cho and Leahy, 2002) and such a constraining CR1/CR2 interaction may not be tolerated in a receptor that does not bind ligand TGFα:sEGFR501.

The 3D structure of ErbB2 also allows the epitopes for monoclonal antibodies to be mapped and their mode of action inferred, since some inhibit, some stimulate and others have no effect on cell growth. The epitopes for mAbs L87, N28 and N12 have been located to the regions Cys199-Cys214, Thr195-Cys214 and Cys510-Ala565 (mature receptor numbering) respectively (Yip YL, Smith G, Koch J, Dubel S, Ward RL. Identification of epitope regions recognized by tumor inhibitory and stimulatory anti-ErbB-2 monoclonal antibodies: implications for vaccine design. J Immunol. 166(8):5271-8, (2001)). The epitopes for mAbs L87 and N28 (reported to have no effect or to stimulate growth of a subset of breast cancer cell lines respectively) are located in the second cys rich module of CR1, while the epitope for mAb N12, an inhibitory antibody, is located within a large region comprising cys rich modules 2 to 4 of CR2 (Figure 2). Similarly the epitope for the potential therapeutic anti-ErbB2 monoclonal antibody MGr6 (Orlandi R, Formantici C, Menard S, Boyer CM, Wiener JR, Colnaghi M. A linear region of a monoclonal antibody conformational epitope mapped on p185HER2 oncoprotein. J. Biol Chem. 378(11):1387-92, (1997)) has been shown to include residues 207-215 (mature receptor numbers) in the third module of CR1.

The CR2 region has also been implicated as the site of action for a set of inhibitory peptides originally designed to mimic the CDR3 loop of herceptin and shown to compete with herceptin for binding to ErbB2. A subsequent set of inhibitory peptides have been designed which mimic sequences in modules 4 to 6 of CR2, a region shown to contribute to ErbB2 heterodimer formation. Other inhibitors of ErbB2 function include the ErbB2 splice variant herstatin and the small, leucine-rich repeat proteoglycan decorin. The inhibition of ErbB2 function in breast cancer cells by decorin has been shown to be indirect and involves inactivation of ErbB4, presumably by direct binding.

The availability of the 3D structures of these receptors will facilitate the determination of the precise mechanism of action of these inhibitory agents and the design of new approaches to interfering with ErbB receptor function.

The disclosure of all publications referred to in this application are incorporated herein by reference.

It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

APPENDIX I

REMARK Coordinates for ErbB2 1-509 construct 25-2.5 A R=0.2258

ATOM	1	CB	SER	1	46.698	22.851	38.977	1.00	99.78
ATOM	2	OG	SER	1	47.614	22.349	39.935	1.00	100.53
ATOM	3	C	SER	1	48.261	24.420	37.763	1.00	98.75
ATOM	4	O	SER	1	48.172	24.394	36.528	1.00	98.79
ATOM	5	N	SER	1	45.832	24.925	37.936	1.00	98.88
ATOM	6	CA	SER	1	47.002	24.314	38.639	1.00	99.43
ATOM	7	N	THR	2	49.431	24.529	38.395	1.00	97.11
ATOM	8	CA	THR	2	50.669	24.691	37.637	1.00	94.13
ATOM	9	CB	THR	2	51.169	26.163	37.747	1.00	94.56
ATOM	10	OG1	THR	2	52.093	26.440	36.686	1.00	94.31
ATOM	11	CG2	THR	2	51.855	26.405	39.098	1.00	94.08
ATOM	12	C	THR	2	51.853	23.755	37.936	1.00	91.66
ATOM	13	O	THR	2	52.049	23.270	39.059	1.00	91.43
ATOM	14	N	GLN	3	52.633	23.530	36.882	1.00	88.14
ATOM	15	CA	GLN	3	53.835	22.705	36.892	1.00	83.26
ATOM	16	CB	GLN	3	53.744	21.659	35.791	1.00	84.63
ATOM	17	CG	GLN	3	53.371	22.279	34.450	1.00	84.29
ATOM	18	CD	GLN	3	53.596	21.346	33.287	1.00	84.81
ATOM	19	OE1	GLN	3	54.731	20.987	32.980	1.00	85.45
ATOM	20	NE2	GLN	3	52.514	20.944	32.631	1.00	84.85
ATOM	21	C	GLN	3	54.972	23.670	36.561	1.00	79.21
ATOM	22	O	GLN	3	56.142	23.289	36.494	1.00	79.22
ATOM	23	N	VAL	4	54.597	24.925	36.338	1.00	73.41
ATOM	24	CA	VAL	4	55.542	25.981	36.003	1.00	68.56
ATOM	25	CB	VAL	4	55.074	26.763	34.752	1.00	68.25
ATOM	26	CG1	VAL	4	55.931	28.002	34.552	1.00	66.99
ATOM	27	CG2	VAL	4	55.139	25.870	33.530	1.00	68.86
ATOM	28	C	VAL	4	55.701	26.972	37.149	1.00	64.66
ATOM	29	O	VAL	4	54.733	27.308	37.832	1.00	65.50
ATOM	30	N	CYS	5	56.927	27.431	37.355	1.00	58.78
ATOM	31	CA	CYS	5	57.212	28.406	38.392	1.00	55.26
ATOM	32	C	CYS	5	58.186	29.414	37.822	1.00	53.65
ATOM	33	O	CYS	5	58.623	29.297	36.680	1.00	54.51
ATOM	34	CB	CYS	5	57.844	27.748	39.614	1.00	55.51
ATOM	35	SG	CYS	5	59.486	27.015	39.305	1.00	53.11
ATOM	36	N	THR	6	58.539	30.401	38.626	1.00	51.73
ATOM	37	CA	THR	6	59.463	31.412	38.176	1.00	52.19
ATOM	38	CB	THR	6	58.830	32.782	38.249	1.00	53.27
ATOM	39	OG1	THR	6	57.717	32.817	37.348	1.00	57.20
ATOM	40	CG2	THR	6	59.849	33.861	37.862	1.00	56.08
ATOM	41	C	THR	6	60.746	31.409	38.979	1.00	51.03
ATOM	42	O	THR	6	60.743	31.182	40.189	1.00	50.21
ATOM	43	N	GLY	7	61.847	31.670	38.290	1.00	48.21
ATOM	44	CA	GLY	7	63.125	31.675	38.960	1.00	47.10
ATOM	45	C	GLY	7	63.314	32.992	39.640	1.00	44.03
ATOM	46	O	GLY	7	62.359	33.713	39.875	1.00	45.91
ATOM	47	N	THR	8	64.556	33.312	39.946	1.00	43.65
ATOM	48	CA	THR	8	64.863	34.561	40.610	1.00	42.53
ATOM	49	CB	THR	8	65.520	34.293	41.963	1.00	44.28
ATOM	50	OG1	THR	8	66.581	33.340	41.802	1.00	46.88
ATOM	51	CG2	THR	8	64.488	33.739	42.943	1.00	47.24
ATOM	52	C	THR	8	65.781	35.417	39.754	1.00	40.10
ATOM	53	O	THR	8	66.004	35.123	38.585	1.00	37.84
ATOM	54	N	ASP	9	66.296	36.485	40.346	1.00	40.12
ATOM	55	CA	ASP	9	67.195	37.394	39.655	1.00	40.60
ATOM	56	CB	ASP	9	66.407	38.434	38.856	1.00	43.09
ATOM	57	CG	ASP	9	67.241	39.086	37.762	1.00	44.32

ATOM	58	OD1	ASP	9	68.488	39.067	37.867	1.00 43.99
ATOM	59	OD2	ASP	9	66.646	39.627	36.804	1.00 45.18
ATOM	60	C	ASP	9	68.023	38.097	40.707	1.00 39.21
ATOM	61	O	ASP	9	68.044	39.318	40.769	1.00 40.86
ATOM	62	N	MET	10	68.704	37.322	41.539	1.00 39.49
ATOM	63	CA	MET	10	69.520	37.896	42.600	1.00 40.57
ATOM	64	CB	MET	10	69.250	37.166	43.915	1.00 40.06
ATOM	65	CG	MET	10	69.796	35.757	43.936	1.00 41.52
ATOM	66	SD	MET	10	68.945	34.741	45.121	1.00 43.89
ATOM	67	CE	MET	10	69.080	35.809	46.633	1.00 45.64
ATOM	68	C	MET	10	71.013	37.836	42.300	1.00 40.42
ATOM	69	O	MET	10	71.811	38.483	42.985	1.00 38.87
ATOM	70	N	LYS	11	71.391	37.059	41.289	1.00 39.91
ATOM	71	CA	LYS	11	72.798	36.926	40.940	1.00 42.86
ATOM	72	CB	LYS	11	73.352	38.252	40.398	1.00 42.49
ATOM	73	CG	LYS	11	72.644	38.787	39.160	1.00 46.76
ATOM	74	CD	LYS	11	72.753	37.820	37.995	1.00 51.31
ATOM	75	CE	LYS	11	72.095	38.371	36.714	1.00 55.51
ATOM	76	NZ	LYS	11	70.623	38.092	36.600	1.00 57.96
ATOM	77	C	LYS	11	73.570	36.517	42.200	1.00 44.00
ATOM	78	O	LYS	11	73.198	35.550	42.877	1.00 43.65
ATOM	79	N	LEU	12	74.624	37.261	42.523	1.00 43.59
ATOM	80	CA	LEU	12	75.438	36.952	43.691	1.00 45.11
ATOM	81	CB	LEU	12	76.919	37.107	43.349	1.00 45.41
ATOM	82	CG	LEU	12	77.420	36.244	42.186	1.00 47.19
ATOM	83	CD1	LEU	12	78.899	36.526	41.919	1.00 44.25
ATOM	84	CD2	LEU	12	77.188	34.778	42.516	1.00 43.16
ATOM	85	C	LEU	12	75.108	37.808	44.912	1.00 46.99
ATOM	86	O	LEU	12	75.836	37.779	45.908	1.00 46.09
ATOM	87	N	ARG	13	74.016	38.571	44.830	1.00 48.04
ATOM	88	CA	ARG	13	73.591	39.427	45.935	1.00 47.76
ATOM	89	CB	ARG	13	72.374	40.279	45.521	1.00 47.43
ATOM	90	CG	ARG	13	72.683	41.496	44.633	1.00 44.43
ATOM	91	CD	ARG	13	71.409	42.038	43.968	1.00 44.08
ATOM	92	NE	ARG	13	71.525	42.039	42.509	1.00 44.91
ATOM	93	CZ	ARG	13	70.526	41.778	41.666	1.00 47.24
ATOM	94	NH1	ARG	13	69.313	41.497	42.130	1.00 43.48
ATOM	95	NH2	ARG	13	70.745	41.763	40.351	1.00 47.70
ATOM	96	C	ARG	13	73.251	38.586	47.177	1.00 49.10
ATOM	97	O	ARG	13	72.547	37.583	47.100	1.00 48.39
ATOM	98	N	LEU	14	73.772	39.019	48.318	1.00 51.74
ATOM	99	CA	LEU	14	73.567	38.353	49.595	1.00 52.86
ATOM	100	CB	LEU	14	74.407	39.058	50.662	1.00 54.52
ATOM	101	CG	LEU	14	74.504	38.400	52.043	1.00 58.51
ATOM	102	CD1	LEU	14	75.513	37.251	51.983	1.00 57.78
ATOM	103	CD2	LEU	14	74.939	39.431	53.088	1.00 58.95
ATOM	104	C	LEU	14	72.101	38.380	50.018	1.00 52.92
ATOM	105	O	LEU	14	71.457	39.420	49.960	1.00 54.88
ATOM	106	N	PRO	15	71.552	37.235	50.447	1.00 52.63
ATOM	107	CD	PRO	15	72.115	35.878	50.477	1.00 53.32
ATOM	108	CA	PRO	15	70.150	37.218	50.872	1.00 52.89
ATOM	109	CB	PRO	15	69.872	35.732	51.119	1.00 53.67
ATOM	110	CG	PRO	15	70.878	35.034	50.267	1.00 54.06
ATOM	111	C	PRO	15	70.063	38.025	52.161	1.00 53.54
ATOM	112	O	PRO	15	70.788	37.738	53.123	1.00 52.81
ATOM	113	N	ALA	16	69.182	39.023	52.181	1.00 54.22
ATOM	114	CA	ALA	16	69.018	39.885	53.355	1.00 54.19
ATOM	115	CB	ALA	16	68.069	41.038	53.032	1.00 54.82
ATOM	116	C	ALA	16	68.521	39.132	54.585	1.00 53.70
ATOM	117	O	ALA	16	68.705	39.587	55.709	1.00 53.21
ATOM	118	N	SER	17	67.902	37.976	54.371	1.00 53.95

ATOM	119	CA	SER	17	67.384	37.181	55.478	1.00	52.73
ATOM	120	CB	SER	17	65.859	37.301	55.521	1.00	51.32
ATOM	121	OG	SER	17	65.320	36.576	56.610	1.00	51.26
ATOM	122	C	SER	17	67.809	35.711	55.351	1.00	52.82
ATOM	123	O	SER	17	67.037	34.853	54.905	1.00	53.32
ATOM	124	N	PRO	18	69.049	35.404	55.755	1.00	52.39
ATOM	125	CD	PRO	18	70.012	36.343	56.358	1.00	52.34
ATOM	126	CA	PRO	18	69.603	34.047	55.697	1.00	51.18
ATOM	127	CB	PRO	18	70.923	34.181	56.442	1.00	52.04
ATOM	128	CG	PRO	18	71.314	35.609	56.181	1.00	53.40
ATOM	129	C	PRO	18	68.704	33.002	56.343	1.00	52.47
ATOM	130	O	PRO	18	68.706	31.832	55.939	1.00	52.40
ATOM	131	N	GLU	19	67.934	33.417	57.346	1.00	52.12
ATOM	132	CA	GLU	19	67.052	32.486	58.045	1.00	52.59
ATOM	133	CB	GLU	19	66.532	33.094	59.354	1.00	56.71
ATOM	134	CG	GLU	19	67.594	33.635	60.310	1.00	63.85
ATOM	135	CD	GLU	19	68.074	35.031	59.930	1.00	68.23
ATOM	136	OE1	GLU	19	67.220	35.871	59.559	1.00	70.68
ATOM	137	OE2	GLU	19	69.298	35.293	60.018	1.00	70.34
ATOM	138	C	GLU	19	65.856	32.036	57.215	1.00	49.61
ATOM	139	O	GLU	19	65.287	30.977	57.478	1.00	48.77
ATOM	140	N	THR	20	65.460	32.835	56.227	1.00	46.30
ATOM	141	CA	THR	20	64.306	32.467	55.411	1.00	44.66
ATOM	142	CB	THR	20	63.179	33.540	55.493	1.00	44.01
ATOM	143	OG1	THR	20	63.700	34.828	55.137	1.00	41.22
ATOM	144	CG2	THR	20	62.603	33.592	56.905	1.00	40.61
ATOM	145	C	THR	20	64.633	32.188	53.952	1.00	42.99
ATOM	146	O	THR	20	63.789	31.708	53.205	1.00	41.80
ATOM	147	N	HIS	21	65.868	32.470	53.560	1.00	43.03
ATOM	148	CA	HIS	21	66.322	32.239	52.191	1.00	43.70
ATOM	149	CB	HIS	21	67.838	32.414	52.104	1.00	43.12
ATOM	150	CG	HIS	21	68.369	32.324	50.708	1.00	42.78
ATOM	151	CD2	HIS	21	69.323	31.530	50.167	1.00	43.08
ATOM	152	ND1	HIS	21	67.918	33.133	49.690	1.00	41.09
ATOM	153	CE1	HIS	21	68.572	32.845	48.580	1.00	42.02
ATOM	154	NE2	HIS	21	69.431	31.874	48.842	1.00	42.45
ATOM	155	C	HIS	21	65.958	30.869	51.619	1.00	43.14
ATOM	156	O	HIS	21	65.452	30.780	50.500	1.00	41.68
ATOM	157	N	LEU	22	66.234	29.811	52.380	1.00	43.54
ATOM	158	CA	LEU	22	65.945	28.442	51.951	1.00	44.32
ATOM	159	CB	LEU	22	66.583	27.434	52.909	1.00	45.68
ATOM	160	CG	LEU	22	66.262	25.962	52.610	1.00	47.25
ATOM	161	CD1	LEU	22	66.790	25.569	51.234	1.00	46.02
ATOM	162	CD2	LEU	22	66.878	25.089	53.676	1.00	46.91
ATOM	163	C	LEU	22	64.457	28.158	51.865	1.00	43.69
ATOM	164	O	LEU	22	63.988	27.439	50.981	1.00	44.10
ATOM	165	N	ASP	23	63.718	28.720	52.804	1.00	45.13
ATOM	166	CA	ASP	23	62.278	28.543	52.861	1.00	45.72
ATOM	167	CB	ASP	23	61.762	29.165	54.159	1.00	48.31
ATOM	168	CG	ASP	23	60.347	28.763	54.483	1.00	52.03
ATOM	169	OD1	ASP	23	59.718	28.037	53.679	1.00	53.43
ATOM	170	OD2	ASP	23	59.861	29.185	55.556	1.00	55.74
ATOM	171	C	ASP	23	61.663	29.215	51.625	1.00	45.83
ATOM	172	O	ASP	23	60.607	28.805	51.124	1.00	46.01
ATOM	173	N	MET	24	62.344	30.241	51.121	1.00	44.06
ATOM	174	CA	MET	24	61.875	30.945	49.937	1.00	41.04
ATOM	175	CB	MET	24	62.681	32.229	49.717	1.00	41.33
ATOM	176	CG	MET	24	62.282	33.010	48.459	1.00	41.54
ATOM	177	SD	MET	24	63.189	32.480	46.990	1.00	41.03
ATOM	178	CE	MET	24	64.724	33.373	47.263	1.00	38.15
ATOM	179	C	MET	24	62.029	30.028	48.746	1.00	39.66

ATOM	180	O	MET	24	61.076	29.809	47.996	1.00	38.86
ATOM	181	N	LEU	25	63.237	29.487	48.585	1.00	39.89
ATOM	182	CA	LEU	25	63.548	28.582	47.479	1.00	39.32
ATOM	183	CB	LEU	25	64.979	28.071	47.609	1.00	38.16
ATOM	184	CG	LEU	25	66.063	29.137	47.425	1.00	38.16
ATOM	185	CD1	LEU	25	67.423	28.570	47.822	1.00	36.13
ATOM	186	CD2	LEU	25	66.061	29.619	45.977	1.00	35.36
ATOM	187	C	LEU	25	62.584	27.412	47.471	1.00	40.05
ATOM	188	O	LEU	25	62.011	27.072	46.437	1.00	41.35
ATOM	189	N	ARG	26	62.409	26.802	48.636	1.00	41.18
ATOM	190	CA	ARG	26	61.502	25.679	48.780	1.00	43.57
ATOM	191	CB	ARG	26	61.430	25.236	50.249	1.00	47.19
ATOM	192	CG	ARG	26	60.308	24.228	50.530	1.00	53.01
ATOM	193	CD	ARG	26	60.193	23.867	52.015	1.00	57.96
ATOM	194	NE	ARG	26	61.417	23.249	52.523	1.00	63.73
ATOM	195	CZ	ARG	26	62.397	23.911	53.135	1.00	67.15
ATOM	196	NH1	ARG	26	62.293	25.222	53.329	1.00	69.09
ATOM	197	NH2	ARG	26	63.492	23.269	53.539	1.00	67.64
ATOM	198	C	ARG	26	60.107	26.045	48.276	1.00	42.82
ATOM	199	O	ARG	26	59.517	25.299	47.497	1.00	42.76
ATOM	200	N	HIS	27	59.580	27.185	48.725	1.00	41.65
ATOM	201	CA	HIS	27	58.249	27.639	48.306	1.00	41.19
ATOM	202	CB	HIS	27	57.892	28.971	48.982	1.00	41.27
ATOM	203	CG	HIS	27	57.358	28.831	50.374	1.00	40.54
ATOM	204	CD2	HIS	27	57.915	29.116	51.575	1.00	39.10
ATOM	205	ND1	HIS	27	56.087	28.363	50.643	1.00	40.15
ATOM	206	CE1	HIS	27	55.887	28.368	51.949	1.00	40.37
ATOM	207	NE2	HIS	27	56.981	28.819	52.537	1.00	37.81
ATOM	208	C	HIS	27	58.244	27.846	46.801	1.00	41.58
ATOM	209	O	HIS	27	57.318	27.455	46.089	1.00	42.62
ATOM	210	N	LEU	28	59.307	28.470	46.328	1.00	42.34
ATOM	211	CA	LEU	28	59.476	28.770	44.920	1.00	44.22
ATOM	212	CB	LEU	28	60.763	29.576	44.750	1.00	46.18
ATOM	213	CG	LEU	28	60.849	30.528	43.572	1.00	46.79
ATOM	214	CD1	LEU	28	59.751	31.570	43.697	1.00	46.45
ATOM	215	CD2	LEU	28	62.221	31.194	43.558	1.00	48.92
ATOM	216	C	LEU	28	59.516	27.554	43.989	1.00	44.27
ATOM	217	O	LEU	28	58.762	27.494	43.016	1.00	45.44
ATOM	218	N	TYR	29	60.377	26.581	44.292	1.00	43.09
ATOM	219	CA	TYR	29	60.534	25.415	43.417	1.00	42.13
ATOM	220	CB	TYR	29	62.022	25.135	43.236	1.00	39.72
ATOM	221	CG	TYR	29	62.757	26.302	42.636	1.00	38.19
ATOM	222	CD1	TYR	29	63.746	26.977	43.353	1.00	34.60
ATOM	223	CE1	TYR	29	64.383	28.101	42.816	1.00	35.85
ATOM	224	CD2	TYR	29	62.420	26.770	41.369	1.00	36.03
ATOM	225	CE2	TYR	29	63.042	27.888	40.825	1.00	38.16
ATOM	226	CZ	TYR	29	64.021	28.554	41.550	1.00	36.60
ATOM	227	OH	TYR	29	64.599	29.683	41.011	1.00	34.62
ATOM	228	C	TYR	29	59.832	24.094	43.717	1.00	43.10
ATOM	229	O	TYR	29	59.749	23.235	42.845	1.00	42.11
ATOM	230	N	GLN	30	59.322	23.914	44.928	1.00	44.62
ATOM	231	CA	GLN	30	58.675	22.651	45.258	1.00	45.73
ATOM	232	CB	GLN	30	58.057	22.722	46.651	1.00	49.77
ATOM	233	CG	GLN	30	57.902	21.367	47.316	1.00	54.17
ATOM	234	CD	GLN	30	57.827	21.494	48.820	1.00	59.15
ATOM	235	OE1	GLN	30	56.949	22.186	49.353	1.00	61.69
ATOM	236	NE2	GLN	30	58.757	20.837	49.523	1.00	60.08
ATOM	237	C	GLN	30	57.616	22.241	44.246	1.00	43.52
ATOM	238	O	GLN	30	56.666	22.971	43.988	1.00	43.46
ATOM	239	N	GLY	31	57.791	21.062	43.670	1.00	42.70
ATOM	240	CA	GLY	31	56.833	20.579	42.698	1.00	44.21

ATOM	241	C	GLY	31	57.004	21.189	41.324	1.00	45.65
ATOM	242	O	GLY	31	56.423	20.704	40.349	1.00	46.11
ATOM	243	N	CYS	32	57.798	22.250	41.232	1.00	45.88
ATOM	244	CA	CYS	32	58.026	22.905	39.946	1.00	47.34
ATOM	245	C	CYS	32	58.777	22.007	38.947	1.00	47.39
ATOM	246	O	CYS	32	59.699	21.272	39.319	1.00	45.44
ATOM	247	CB	CYS	32	58.819	24.193	40.147	1.00	48.51
ATOM	248	SG	CYS	32	58.990	25.178	38.624	1.00	50.51
ATOM	249	N	GLN	33	58.378	22.078	37.679	1.00	47.35
ATOM	250	CA	GLN	33	59.012	21.292	36.620	1.00	48.75
ATOM	251	CB	GLN	33	57.989	20.400	35.932	1.00	49.20
ATOM	252	CG	GLN	33	57.576	19.204	36.755	1.00	54.87
ATOM	253	CD	GLN	33	56.562	18.341	36.036	1.00	57.52
ATOM	254	OE1	GLN	33	56.554	17.117	36.185	1.00	57.65
ATOM	255	NE2	GLN	33	55.690	18.978	35.255	1.00	58.17
ATOM	256	C	GLN	33	59.679	22.183	35.572	1.00	49.12
ATOM	257	O	GLN	33	60.759	21.859	35.066	1.00	48.02
ATOM	258	N	VAL	34	59.024	23.296	35.240	1.00	47.34
ATOM	259	CA	VAL	34	59.559	24.236	34.260	1.00	44.43
ATOM	260	CB	VAL	34	58.583	24.448	33.091	1.00	42.79
ATOM	261	CG1	VAL	34	59.141	25.488	32.129	1.00	42.57
ATOM	262	CG2	VAL	34	58.355	23.141	32.369	1.00	39.31
ATOM	263	C	VAL	34	59.817	25.577	34.930	1.00	44.27
ATOM	264	O	VAL	34	58.895	26.216	35.424	1.00	46.02
ATOM	265	N	VAL	35	61.073	25.998	34.946	1.00	42.27
ATOM	266	CA	VAL	35	61.434	27.255	35.568	1.00	42.31
ATOM	267	CB	VAL	35	62.742	27.117	36.360	1.00	41.24
ATOM	268	CG1	VAL	35	63.170	28.473	36.909	1.00	40.12
ATOM	269	CG2	VAL	35	62.555	26.125	37.480	1.00	39.17
ATOM	270	C	VAL	35	61.601	28.409	34.583	1.00	43.64
ATOM	271	O	VAL	35	62.617	28.494	33.890	1.00	42.15
ATOM	272	N	GLN	36	60.591	29.276	34.511	1.00	45.54
ATOM	273	CA	GLN	36	60.666	30.453	33.653	1.00	48.03
ATOM	274	CB	GLN	36	59.339	31.226	33.650	1.00	52.27
ATOM	275	CG	GLN	36	58.117	30.387	33.323	1.00	58.81
ATOM	276	CD	GLN	36	58.043	29.982	31.861	1.00	62.93
ATOM	277	OE1	GLN	36	59.060	29.949	31.155	1.00	66.35
ATOM	278	NE2	GLN	36	56.837	29.651	31.402	1.00	63.08
ATOM	279	C	GLN	36	61.714	31.268	34.398	1.00	46.27
ATOM	280	O	GLN	36	61.757	31.237	35.630	1.00	49.00
ATOM	281	N	GLY	37	62.567	31.989	33.694	1.00	41.30
ATOM	282	CA	GLY	37	63.556	32.739	34.437	1.00	40.34
ATOM	283	C	GLY	37	64.762	31.895	34.812	1.00	39.23
ATOM	284	O	GLY	37	65.041	30.870	34.187	1.00	39.87
ATOM	285	N	ASN	38	65.466	32.305	35.853	1.00	37.71
ATOM	286	CA	ASN	38	66.681	31.617	36.253	1.00	37.65
ATOM	287	CB	ASN	38	67.796	32.647	36.355	1.00	38.08
ATOM	288	CG	ASN	38	67.723	33.667	35.259	1.00	40.43
ATOM	289	OD1	ASN	38	67.923	33.356	34.087	1.00	40.88
ATOM	290	ND2	ASN	38	67.412	34.897	35.628	1.00	42.58
ATOM	291	C	ASN	38	66.645	30.809	37.542	1.00	37.32
ATOM	292	O	ASN	38	65.976	31.175	38.509	1.00	37.72
ATOM	293	N	LEU	39	67.385	29.706	37.543	1.00	35.57
ATOM	294	CA	LEU	39	67.488	28.861	38.719	1.00	36.14
ATOM	295	CB	LEU	39	67.563	27.386	38.334	1.00	35.37
ATOM	296	CG	LEU	39	67.785	26.494	39.559	1.00	36.47
ATOM	297	CD1	LEU	39	66.662	26.738	40.561	1.00	36.90
ATOM	298	CD2	LEU	39	67.840	25.027	39.153	1.00	33.34
ATOM	299	C	LEU	39	68.776	29.274	39.411	1.00	37.41
ATOM	300	O	LEU	39	69.873	28.952	38.933	1.00	36.96
ATOM	301	N	GLU	40	68.644	29.998	40.524	1.00	37.19

ATOM	302	CA	GLU	40	69.808	30.471	41.266	1.00	38.08
ATOM	303	CB	GLU	40	69.806	32.003	41.350	1.00	38.80
ATOM	304	CG	GLU	40	69.494	32.703	40.013	1.00	42.78
ATOM	305	CD	GLU	40	69.452	34.223	40.117	1.00	41.78
ATOM	306	OE1	GLU	40	70.459	34.885	39.779	1.00	43.35
ATOM	307	OE2	GLU	40	68.411	34.755	40.546	1.00	42.97
ATOM	308	C	GLU	40	69.846	29.875	42.666	1.00	39.52
ATOM	309	O	GLU	40	69.009	30.185	43.509	1.00	38.50
ATOM	310	N	LEU	41	70.826	29.005	42.893	1.00	40.86
ATOM	311	CA	LEU	41	71.017	28.346	44.173	1.00	41.39
ATOM	312	CB	LEU	41	71.104	26.846	43.942	1.00	41.49
ATOM	313	CG	LEU	41	69.800	26.337	43.304	1.00	42.78
ATOM	314	CD1	LEU	41	69.983	24.930	42.767	1.00	39.41
ATOM	315	CD2	LEU	41	68.667	26.390	44.342	1.00	40.37
ATOM	316	C	LEU	41	72.302	28.895	44.784	1.00	43.48
ATOM	317	O	LEU	41	73.414	28.483	44.423	1.00	43.60
ATOM	318	N	THR	42	72.137	29.837	45.711	1.00	42.93
ATOM	319	CA	THR	42	73.271	30.494	46.337	1.00	42.71
ATOM	320	CB	THR	42	73.405	31.940	45.809	1.00	42.41
ATOM	321	OG1	THR	42	72.214	32.679	46.124	1.00	44.65
ATOM	322	CG2	THR	42	73.597	31.940	44.299	1.00	40.36
ATOM	323	C	THR	42	73.228	30.547	47.859	1.00	44.56
ATOM	324	O	THR	42	72.170	30.371	48.474	1.00	44.84
ATOM	325	N	TYR	43	74.402	30.793	48.444	1.00	45.06
ATOM	326	CA	TYR	43	74.599	30.912	49.889	1.00	45.25
ATOM	327	CB	TYR	43	74.222	32.326	50.355	1.00	43.21
ATOM	328	CG	TYR	43	75.011	33.417	49.663	1.00	45.31
ATOM	329	CD1	TYR	43	74.534	34.021	48.495	1.00	44.65
ATOM	330	CE1	TYR	43	75.295	34.970	47.809	1.00	44.72
ATOM	331	CD2	TYR	43	76.271	33.795	50.133	1.00	46.31
ATOM	332	CE2	TYR	43	77.047	34.742	49.452	1.00	45.38
ATOM	333	CZ	TYR	43	76.557	35.323	48.291	1.00	46.22
ATOM	334	OH	TYR	43	77.342	36.227	47.598	1.00	42.92
ATOM	335	C	TYR	43	73.883	29.886	50.768	1.00	46.52
ATOM	336	O	TYR	43	73.432	30.216	51.864	1.00	46.70
ATOM	337	N	LEU	44	73.795	28.645	50.310	1.00	47.21
ATOM	338	CA	LEU	44	73.126	27.622	51.098	1.00	50.64
ATOM	339	CB	LEU	44	72.463	26.592	50.181	1.00	49.29
ATOM	340	CG	LEU	44	71.380	27.177	49.271	1.00	47.48
ATOM	341	CD1	LEU	44	70.697	26.077	48.489	1.00	47.96
ATOM	342	CD2	LEU	44	70.371	27.914	50.117	1.00	46.43
ATOM	343	C	LEU	44	74.098	26.931	52.044	1.00	53.36
ATOM	344	O	LEU	44	75.175	26.517	51.634	1.00	53.59
ATOM	345	N	PRO	45	73.725	26.807	53.334	1.00	56.73
ATOM	346	CD	PRO	45	72.430	27.232	53.900	1.00	58.00
ATOM	347	CA	PRO	45	74.548	26.168	54.368	1.00	57.37
ATOM	348	CB	PRO	45	73.802	26.506	55.652	1.00	57.48
ATOM	349	CG	PRO	45	72.373	26.447	55.205	1.00	59.17
ATOM	350	C	PRO	45	74.677	24.659	54.141	1.00	58.12
ATOM	351	O	PRO	45	73.874	24.053	53.425	1.00	57.47
ATOM	352	N	THR	46	75.680	24.060	54.772	1.00	57.76
ATOM	353	CA	THR	46	75.945	22.641	54.610	1.00	57.98
ATOM	354	CB	THR	46	77.255	22.257	55.363	1.00	56.25
ATOM	355	OG1	THR	46	77.894	21.172	54.683	1.00	57.72
ATOM	356	CG2	THR	46	76.972	21.841	56.791	1.00	55.98
ATOM	357	C	THR	46	74.799	21.696	55.003	1.00	59.34
ATOM	358	O	THR	46	74.720	20.572	54.508	1.00	59.26
ATOM	359	N	ASN	47	73.895	22.147	55.864	1.00	62.38
ATOM	360	CA	ASN	47	72.791	21.291	56.300	1.00	66.35
ATOM	361	CB	ASN	47	72.480	21.549	57.781	1.00	72.57
ATOM	362	CG	ASN	47	72.136	23.006	58.064	1.00	78.54

ATOM	363	OD1	ASN	47	71.287	23.596	57.391	1.00	79.41
ATOM	364	ND2	ASN	47	72.792	23.586	59.066	1.00	83.60
ATOM	365	C	ASN	47	71.509	21.462	55.488	1.00	65.90
ATOM	366	O	ASN	47	70.466	20.906	55.838	1.00	66.68
ATOM	367	N	ALA	48	71.593	22.218	54.398	1.00	64.94
ATOM	368	CA	ALA	48	70.435	22.491	53.549	1.00	61.77
ATOM	369	CB	ALA	48	70.783	23.582	52.548	1.00	61.89
ATOM	370	C	ALA	48	69.845	21.294	52.813	1.00	60.59
ATOM	371	O	ALA	48	70.524	20.630	52.030	1.00	60.88
ATOM	372	N	SER	49	68.572	21.022	53.075	1.00	58.17
ATOM	373	CA	SER	49	67.875	19.937	52.405	1.00	57.25
ATOM	374	CB	SER	49	66.781	19.367	53.304	1.00	59.13
ATOM	375	OG	SER	49	65.951	18.483	52.566	1.00	62.13
ATOM	376	C	SER	49	67.245	20.536	51.150	1.00	55.84
ATOM	377	O	SER	49	66.339	21.365	51.247	1.00	56.85
ATOM	378	N	LEU	50	67.710	20.099	49.983	1.00	53.85
ATOM	379	CA	LEU	50	67.236	20.609	48.702	1.00	50.83
ATOM	380	CB	LEU	50	68.432	21.048	47.872	1.00	48.70
ATOM	381	CG	LEU	50	69.386	22.023	48.554	1.00	50.27
ATOM	382	CD1	LEU	50	70.539	22.339	47.601	1.00	48.46
ATOM	383	CD2	LEU	50	68.635	23.298	48.948	1.00	50.37
ATOM	384	C	LEU	50	66.396	19.651	47.863	1.00	50.80
ATOM	385	O	LEU	50	66.304	19.812	46.652	1.00	51.99
ATOM	386	N	SER	51	65.777	18.666	48.492	1.00	50.31
ATOM	387	CA	SER	51	64.972	17.696	47.758	1.00	49.12
ATOM	388	CB	SER	51	64.342	16.710	48.737	1.00	49.94
ATOM	389	OG	SER	51	63.326	17.355	49.486	1.00	54.77
ATOM	390	C	SER	51	63.861	18.311	46.897	1.00	48.09
ATOM	391	O	SER	51	63.420	17.710	45.920	1.00	49.53
ATOM	392	N	PHE	52	63.398	19.500	47.252	1.00	45.59
ATOM	393	CA	PHE	52	62.330	20.121	46.487	1.00	44.82
ATOM	394	CB	PHE	52	61.796	21.335	47.245	1.00	45.04
ATOM	395	CG	PHE	52	62.850	22.338	47.608	1.00	44.14
ATOM	396	CD1	PHE	52	63.365	23.208	46.652	1.00	41.89
ATOM	397	CD2	PHE	52	63.322	22.424	48.919	1.00	43.61
ATOM	398	CE1	PHE	52	64.342	24.158	47.000	1.00	40.61
ATOM	399	CE2	PHE	52	64.300	23.368	49.275	1.00	41.30
ATOM	400	CZ	PHE	52	64.806	24.235	48.313	1.00	39.55
ATOM	401	C	PHE	52	62.712	20.520	45.059	1.00	44.76
ATOM	402	O	PHE	52	61.859	20.959	44.289	1.00	44.08
ATOM	403	N	LEU	53	63.986	20.360	44.710	1.00	43.96
ATOM	404	CA	LEU	53	64.485	20.701	43.382	1.00	43.72
ATOM	405	CB	LEU	53	65.931	21.183	43.481	1.00	40.39
ATOM	406	CG	LEU	53	66.283	22.422	44.307	1.00	40.76
ATOM	407	CD1	LEU	53	67.788	22.494	44.453	1.00	39.34
ATOM	408	CD2	LEU	53	65.757	23.691	43.631	1.00	40.38
ATOM	409	C	LEU	53	64.449	19.506	42.419	1.00	46.76
ATOM	410	O	LEU	53	64.773	19.643	41.233	1.00	47.47
ATOM	411	N	GLN	54	64.048	18.343	42.927	1.00	48.46
ATOM	412	CA	GLN	54	64.029	17.108	42.140	1.00	49.89
ATOM	413	CB	GLN	54	63.710	15.913	43.050	1.00	52.52
ATOM	414	CG	GLN	54	62.363	16.008	43.756	1.00	57.71
ATOM	415	CD	GLN	54	61.976	14.718	44.471	1.00	60.56
ATOM	416	OE1	GLN	54	62.778	14.139	45.213	1.00	59.21
ATOM	417	NE2	GLN	54	60.735	14.269	44.259	1.00	61.81
ATOM	418	C	GLN	54	63.138	17.026	40.904	1.00	48.57
ATOM	419	O	GLN	54	63.359	16.159	40.050	1.00	47.17
ATOM	420	N	ASP	55	62.147	17.907	40.786	1.00	47.48
ATOM	421	CA	ASP	55	61.248	17.853	39.630	1.00	47.88
ATOM	422	CB	ASP	55	59.814	18.076	40.082	1.00	51.15
ATOM	423	CG	ASP	55	59.371	17.062	41.089	1.00	55.30

ATOM	424	OD1	ASP	55	59.391	15.852	40.759	1.00	55.97
ATOM	425	OD2	ASP	55	59.012	17.480	42.213	1.00	58.38
ATOM	426	C	ASP	55	61.557	18.801	38.475	1.00	46.37
ATOM	427	O	ASP	55	60.917	18.725	37.423	1.00	47.17
ATOM	428	N	ILE	56	62.523	19.693	38.672	1.00	44.29
ATOM	429	CA	ILE	56	62.928	20.648	37.643	1.00	43.21
ATOM	430	CB	ILE	56	64.033	21.585	38.197	1.00	40.52
ATOM	431	CG2	ILE	56	64.534	22.528	37.117	1.00	37.41
ATOM	432	CG1	ILE	56	63.486	22.350	39.401	1.00	37.70
ATOM	433	CD1	ILE	56	64.501	23.185	40.099	1.00	37.33
ATOM	434	C	ILE	56	63.453	19.887	36.409	1.00	44.92
ATOM	435	O	ILE	56	64.379	19.077	36.516	1.00	45.32
ATOM	436	N	GLN	57	62.842	20.139	35.254	1.00	44.74
ATOM	437	CA	GLN	57	63.225	19.496	33.998	1.00	46.02
ATOM	438	CB	GLN	57	62.017	18.887	33.307	1.00	48.48
ATOM	439	CG	GLN	57	61.555	17.577	33.863	1.00	54.00
ATOM	440	CD	GLN	57	60.559	16.928	32.937	1.00	56.38
ATOM	441	OE1	GLN	57	60.682	17.034	31.713	1.00	58.36
ATOM	442	NE2	GLN	57	59.572	16.245	33.505	1.00	57.50
ATOM	443	C	GLN	57	63.862	20.473	33.027	1.00	45.57
ATOM	444	O	GLN	57	64.740	20.100	32.249	1.00	44.05
ATOM	445	N	GLU	58	63.377	21.711	33.033	1.00	45.73
ATOM	446	CA	GLU	58	63.934	22.738	32.169	1.00	45.78
ATOM	447	CB	GLU	58	63.166	22.825	30.844	1.00	48.71
ATOM	448	CG	GLU	58	61.654	22.860	30.928	1.00	53.11
ATOM	449	CD	GLU	58	60.996	22.732	29.546	1.00	56.02
ATOM	450	OE1	GLU	58	61.070	21.635	28.932	1.00	53.20
ATOM	451	OE2	GLU	58	60.410	23.737	29.072	1.00	58.53
ATOM	452	C	GLU	58	63.998	24.099	32.844	1.00	43.99
ATOM	453	O	GLU	58	63.206	24.406	33.729	1.00	43.84
ATOM	454	N	VAL	59	64.985	24.888	32.445	1.00	42.10
ATOM	455	CA	VAL	59	65.180	26.224	32.982	1.00	41.08
ATOM	456	CB	VAL	59	66.464	26.297	33.820	1.00	38.49
ATOM	457	CG1	VAL	59	66.931	27.751	33.959	1.00	36.98
ATOM	458	CG2	VAL	59	66.212	25.680	35.189	1.00	36.83
ATOM	459	C	VAL	59	65.291	27.164	31.786	1.00	43.13
ATOM	460	O	VAL	59	66.204	27.025	30.968	1.00	43.59
ATOM	461	N	GLN	60	64.355	28.107	31.685	1.00	43.10
ATOM	462	CA	GLN	60	64.335	29.048	30.577	1.00	44.01
ATOM	463	CB	GLN	60	63.006	29.797	30.573	1.00	48.84
ATOM	464	CG	GLN	60	62.831	30.739	29.394	1.00	52.91
ATOM	465	CD	GLN	60	62.559	32.139	29.866	1.00	57.79
ATOM	466	OE1	GLN	60	61.503	32.414	30.436	1.00	60.40
ATOM	467	NE2	GLN	60	63.523	33.037	29.659	1.00	60.28
ATOM	468	C	GLN	60	65.510	30.033	30.592	1.00	43.30
ATOM	469	O	GLN	60	66.031	30.416	29.537	1.00	41.41
ATOM	470	N	GLY	61	65.928	30.441	31.786	1.00	42.03
ATOM	471	CA	GLY	61	67.053	31.352	31.892	1.00	40.78
ATOM	472	C	GLY	61	68.354	30.577	32.012	1.00	40.97
ATOM	473	O	GLY	61	68.605	29.643	31.246	1.00	40.44
ATOM	474	N	TYR	62	69.180	30.970	32.978	1.00	40.18
ATOM	475	CA	TYR	62	70.459	30.319	33.237	1.00	40.06
ATOM	476	CB	TYR	62	71.589	31.350	33.229	1.00	39.70
ATOM	477	CG	TYR	62	71.461	32.427	34.287	1.00	39.27
ATOM	478	CD1	TYR	62	71.835	32.188	35.610	1.00	38.87
ATOM	479	CE1	TYR	62	71.724	33.190	36.589	1.00	39.73
ATOM	480	CD2	TYR	62	70.965	33.698	33.960	1.00	40.72
ATOM	481	CE2	TYR	62	70.847	34.710	34.925	1.00	40.09
ATOM	482	CZ	TYR	62	71.227	34.448	36.239	1.00	41.39
ATOM	483	OH	TYR	62	71.094	35.431	37.197	1.00	39.21
ATOM	484	C	TYR	62	70.410	29.634	34.598	1.00	40.89

ATOM	485	O	TYR	62	69.461	29.823	35.361	1.00	41.00
ATOM	486	N	VAL	63	71.439	28.841	34.896	1.00	41.43
ATOM	487	CA	VAL	63	71.530	28.122	36.167	1.00	39.60
ATOM	488	CB	VAL	63	71.634	26.596	35.959	1.00	37.74
ATOM	489	CG1	VAL	63	71.827	25.916	37.298	1.00	36.52
ATOM	490	CG2	VAL	63	70.376	26.063	35.276	1.00	37.06
ATOM	491	C	VAL	63	72.759	28.568	36.944	1.00	40.62
ATOM	492	O	VAL	63	73.886	28.332	36.526	1.00	40.79
ATOM	493	N	LEU	64	72.532	29.210	38.083	1.00	42.23
ATOM	494	CA	LEU	64	73.613	29.689	38.928	1.00	41.00
ATOM	495	CB	LEU	64	73.435	31.182	39.213	1.00	41.07
ATOM	496	CG	LEU	64	74.493	31.862	40.092	1.00	42.23
ATOM	497	CD1	LEU	64	75.867	31.792	39.419	1.00	37.35
ATOM	498	CD2	LEU	64	74.070	33.317	40.343	1.00	37.32
ATOM	499	C	LEU	64	73.605	28.906	40.232	1.00	42.23
ATOM	500	O	LEU	64	72.571	28.781	40.894	1.00	41.03
ATOM	501	N	ILE	65	74.766	28.361	40.574	1.00	42.40
ATOM	502	CA	ILE	65	74.960	27.587	41.791	1.00	41.32
ATOM	503	CB	ILE	65	75.166	26.101	41.494	1.00	39.96
ATOM	504	CG2	ILE	65	75.532	25.368	42.783	1.00	41.29
ATOM	505	CG1	ILE	65	73.906	25.517	40.855	1.00	40.19
ATOM	506	CD1	ILE	65	74.037	24.057	40.414	1.00	36.26
ATOM	507	C	ILE	65	76.255	28.140	42.336	1.00	42.20
ATOM	508	O	ILE	65	77.323	27.816	41.827	1.00	42.24
ATOM	509	N	ALA	66	76.173	28.976	43.363	1.00	43.21
ATOM	510	CA	ALA	66	77.383	29.579	43.892	1.00	44.14
ATOM	511	CB	ALA	66	77.696	30.853	43.103	1.00	39.19
ATOM	512	C	ALA	66	77.348	29.890	45.379	1.00	46.15
ATOM	513	O	ALA	66	76.285	30.089	45.963	1.00	46.35
ATOM	514	N	HIS	67	78.537	29.936	45.976	1.00	48.07
ATOM	515	CA	HIS	67	78.697	30.243	47.386	1.00	49.29
ATOM	516	CB	HIS	67	78.336	31.705	47.636	1.00	51.64
ATOM	517	CG	HIS	67	79.390	32.669	47.190	1.00	54.81
ATOM	518	CD2	HIS	67	79.392	33.596	46.203	1.00	56.63
ATOM	519	ND1	HIS	67	80.625	32.753	47.797	1.00	57.63
ATOM	520	CE1	HIS	67	81.343	33.692	47.205	1.00	57.69
ATOM	521	NE2	HIS	67	80.617	34.219	46.234	1.00	57.89
ATOM	522	C	HIS	67	77.892	29.338	48.305	1.00	49.42
ATOM	523	O	HIS	67	77.306	29.786	49.289	1.00	50.64
ATOM	524	N	ASN	68	77.871	28.055	47.987	1.00	49.48
ATOM	525	CA	ASN	68	77.147	27.111	48.810	1.00	49.88
ATOM	526	CB	ASN	68	76.222	26.266	47.942	1.00	48.94
ATOM	527	CG	ASN	68	75.243	27.113	47.157	1.00	50.57
ATOM	528	OD1	ASN	68	74.477	27.890	47.737	1.00	48.22
ATOM	529	ND2	ASN	68	75.266	26.977	45.830	1.00	48.81
ATOM	530	C	ASN	68	78.135	26.222	49.543	1.00	51.48
ATOM	531	O	ASN	68	79.266	26.020	49.093	1.00	51.22
ATOM	532	N	GLN	69	77.704	25.713	50.689	1.00	52.43
ATOM	533	CA	GLN	69	78.525	24.825	51.488	1.00	53.43
ATOM	534	CB	GLN	69	78.554	25.292	52.944	1.00	55.53
ATOM	535	CG	GLN	69	79.220	26.638	53.133	1.00	60.31
ATOM	536	CD	GLN	69	80.547	26.714	52.402	1.00	64.35
ATOM	537	OE1	GLN	69	81.401	25.840	52.559	1.00	66.60
ATOM	538	NE2	GLN	69	80.728	27.759	51.595	1.00	65.26
ATOM	539	C	GLN	69	77.910	23.439	51.390	1.00	52.50
ATOM	540	O	GLN	69	78.518	22.450	51.788	1.00	55.45
ATOM	541	N	VAL	70	76.698	23.375	50.848	1.00	49.65
ATOM	542	CA	VAL	70	75.990	22.112	50.689	1.00	47.14
ATOM	543	CB	VAL	70	74.576	22.365	50.098	1.00	45.05
ATOM	544	CG1	VAL	70	74.673	22.681	48.614	1.00	43.90
ATOM	545	CG2	VAL	70	73.676	21.176	50.366	1.00	45.15

ATOM	546	C	VAL	70	76.814	21.173	49.787	1.00	47.49
ATOM	547	O	VAL	70	77.539	21.622	48.905	1.00	44.75
ATOM	548	N	ARG	71	76.702	19.869	50.002	1.00	50.39
ATOM	549	CA	ARG	71	77.497	18.931	49.219	1.00	55.11
ATOM	550	CB	ARG	71	77.877	17.720	50.078	1.00	56.84
ATOM	551	CG	ARG	71	78.651	18.115	51.328	1.00	60.61
ATOM	552	CD	ARG	71	79.305	16.937	52.011	1.00	63.62
ATOM	553	NE	ARG	71	79.895	17.351	53.279	1.00	67.41
ATOM	554	CZ	ARG	71	79.191	17.586	54.383	1.00	70.48
ATOM	555	NH1	ARG	71	77.869	17.439	54.377	1.00	71.09
ATOM	556	NH2	ARG	71	79.806	17.984	55.490	1.00	70.91
ATOM	557	C	ARG	71	76.874	18.470	47.916	1.00	56.48
ATOM	558	O	ARG	71	77.592	18.082	46.984	1.00	55.56
ATOM	559	N	GLN	72	75.546	18.511	47.846	1.00	57.00
ATOM	560	CA	GLN	72	74.855	18.110	46.632	1.00	56.93
ATOM	561	CB	GLN	72	74.520	16.616	46.662	1.00	57.34
ATOM	562	CG	GLN	72	73.595	16.185	45.505	1.00	61.22
ATOM	563	CD	GLN	72	74.186	16.421	44.097	1.00	62.35
ATOM	564	OE1	GLN	72	74.791	17.467	43.810	1.00	59.65
ATOM	565	NE2	GLN	72	73.988	15.444	43.210	1.00	63.04
ATOM	566	C	GLN	72	73.582	18.902	46.365	1.00	55.55
ATOM	567	O	GLN	72	72.872	19.300	47.284	1.00	55.69
ATOM	568	N	VAL	73	73.319	19.124	45.082	1.00	54.03
ATOM	569	CA	VAL	73	72.147	19.842	44.608	1.00	52.00
ATOM	570	CB	VAL	73	72.571	21.137	43.888	1.00	52.61
ATOM	571	CG1	VAL	73	73.274	22.065	44.869	1.00	51.82
ATOM	572	CG2	VAL	73	73.537	20.806	42.753	1.00	57.12
ATOM	573	C	VAL	73	71.460	18.881	43.637	1.00	50.04
ATOM	574	O	VAL	73	71.853	18.758	42.489	1.00	49.44
ATOM	575	N	PRO	74	70.425	18.173	44.103	1.00	50.40
ATOM	576	CD	PRO	74	69.847	18.290	45.453	1.00	49.59
ATOM	577	CA	PRO	74	69.670	17.202	43.304	1.00	50.32
ATOM	578	CB	PRO	74	68.715	16.589	44.330	1.00	50.82
ATOM	579	CG	PRO	74	68.455	17.735	45.253	1.00	50.68
ATOM	580	C	PRO	74	68.936	17.697	42.056	1.00	49.40
ATOM	581	O	PRO	74	67.708	17.846	42.051	1.00	50.49
ATOM	582	N	LEU	75	69.694	17.925	40.991	1.00	47.89
ATOM	583	CA	LEU	75	69.124	18.366	39.724	1.00	46.86
ATOM	584	CB	LEU	75	69.824	19.644	39.254	1.00	43.48
ATOM	585	CG	LEU	75	69.457	20.850	40.125	1.00	43.50
ATOM	586	CD1	LEU	75	70.382	22.007	39.846	1.00	40.95
ATOM	587	CD2	LEU	75	68.004	21.235	39.862	1.00	42.32
ATOM	588	C	LEU	75	69.253	17.264	38.675	1.00	46.45
ATOM	589	O	LEU	75	69.535	17.541	37.510	1.00	46.20
ATOM	590	N	GLN	76	69.034	16.016	39.094	1.00	47.00
ATOM	591	CA	GLN	76	69.138	14.871	38.191	1.00	46.56
ATOM	592	CB	GLN	76	69.037	13.545	38.949	1.00	48.03
ATOM	593	CG	GLN	76	70.267	13.160	39.761	1.00	52.56
ATOM	594	CD	GLN	76	70.356	13.903	41.088	1.00	54.82
ATOM	595	OE1	GLN	76	69.411	14.601	41.485	1.00	56.30
ATOM	596	NE2	GLN	76	71.486	13.746	41.789	1.00	51.88
ATOM	597	C	GLN	76	68.128	14.842	37.054	1.00	45.92
ATOM	598	O	GLN	76	68.341	14.118	36.087	1.00	46.57
ATOM	599	N	ARG	77	67.037	15.605	37.145	1.00	44.53
ATOM	600	CA	ARG	77	66.058	15.592	36.053	1.00	42.84
ATOM	601	CB	ARG	77	64.645	15.385	36.586	1.00	45.72
ATOM	602	CG	ARG	77	64.453	14.065	37.281	1.00	50.95
ATOM	603	CD	ARG	77	62.984	13.699	37.368	1.00	55.58
ATOM	604	NE	ARG	77	62.768	12.654	38.363	1.00	61.00
ATOM	605	CZ	ARG	77	62.080	12.832	39.487	1.00	64.13
ATOM	606	NH1	ARG	77	61.538	14.017	39.746	1.00	65.36

ATOM	607	NH2	ARG	77	61.940	11.835	40.357	1.00	64.68
ATOM	608	C	ARG	77	66.083	16.825	35.155	1.00	40.56
ATOM	609	O	ARG	77	65.224	16.997	34.288	1.00	38.61
ATOM	610	N	LEU	78	67.068	17.687	35.361	1.00	38.63
ATOM	611	CA	LEU	78	67.191	18.877	34.539	1.00	37.84
ATOM	612	CB	LEU	78	68.222	19.828	35.133	1.00	35.63
ATOM	613	CG	LEU	78	68.500	21.074	34.304	1.00	34.86
ATOM	614	CD1	LEU	78	67.195	21.841	34.072	1.00	33.94
ATOM	615	CD2	LEU	78	69.524	21.923	35.024	1.00	32.14
ATOM	616	C	LEU	78	67.631	18.424	33.157	1.00	39.74
ATOM	617	O	LEU	78	68.751	17.947	32.968	1.00	38.58
ATOM	618	N	ARG	79	66.731	18.563	32.194	1.00	42.07
ATOM	619	CA	ARG	79	67.001	18.154	30.824	1.00	43.44
ATOM	620	CB	ARG	79	65.719	17.640	30.186	1.00	44.33
ATOM	621	CG	ARG	79	65.967	16.780	29.007	1.00	49.41
ATOM	622	CD	ARG	79	66.291	15.400	29.506	1.00	57.39
ATOM	623	NE	ARG	79	67.309	14.738	28.707	1.00	58.07
ATOM	624	CZ	ARG	79	67.735	13.513	28.956	1.00	60.12
ATOM	625	NH1	ARG	79	67.215	12.848	29.977	1.00	61.40
ATOM	626	NH2	ARG	79	68.677	12.965	28.198	1.00	62.59
ATOM	627	C	ARG	79	67.554	19.259	29.925	1.00	44.07
ATOM	628	O	ARG	79	68.445	19.024	29.110	1.00	46.42
ATOM	629	N	ILE	80	67.034	20.469	30.074	1.00	44.22
ATOM	630	CA	ILE	80	67.449	21.547	29.197	1.00	44.40
ATOM	631	CB	ILE	80	66.516	21.562	27.968	1.00	45.97
ATOM	632	CG2	ILE	80	65.072	21.389	28.421	1.00	45.82
ATOM	633	CG1	ILE	80	66.676	22.857	27.179	1.00	47.04
ATOM	634	CD1	ILE	80	65.668	22.989	26.046	1.00	49.16
ATOM	635	C	ILE	80	67.473	22.937	29.813	1.00	43.53
ATOM	636	O	ILE	80	66.607	23.297	30.606	1.00	46.12
ATOM	637	N	VAL	81	68.492	23.707	29.453	1.00	41.12
ATOM	638	CA	VAL	81	68.617	25.078	29.909	1.00	39.98
ATOM	639	CB	VAL	81	69.940	25.317	30.637	1.00	37.75
ATOM	640	CG1	VAL	81	70.063	26.790	31.019	1.00	33.86
ATOM	641	CG2	VAL	81	70.005	24.441	31.880	1.00	37.92
ATOM	642	C	VAL	81	68.591	25.895	28.622	1.00	41.11
ATOM	643	O	VAL	81	69.516	25.805	27.817	1.00	41.60
ATOM	644	N	ARG	82	67.525	26.669	28.422	1.00	40.63
ATOM	645	CA	ARG	82	67.366	27.474	27.213	1.00	41.36
ATOM	646	CB	ARG	82	65.906	27.914	27.057	1.00	41.22
ATOM	647	CG	ARG	82	64.970	26.741	26.805	1.00	41.15
ATOM	648	CD	ARG	82	63.507	27.152	26.721	1.00	39.21
ATOM	649	NE	ARG	82	62.642	25.974	26.746	1.00	39.74
ATOM	650	CZ	ARG	82	62.532	25.094	25.755	1.00	37.15
ATOM	651	NH1	ARG	82	63.223	25.249	24.641	1.00	36.57
ATOM	652	NH2	ARG	82	61.735	24.047	25.888	1.00	39.83
ATOM	653	C	ARG	82	68.279	28.682	27.126	1.00	40.96
ATOM	654	O	ARG	82	68.615	29.123	26.035	1.00	43.30
ATOM	655	N	GLY	83	68.677	29.222	28.267	1.00	41.75
ATOM	656	CA	GLY	83	69.573	30.363	28.252	1.00	42.37
ATOM	657	C	GLY	83	69.023	31.619	27.601	1.00	43.59
ATOM	658	O	GLY	83	69.744	32.317	26.878	1.00	41.39
ATOM	659	N	THR	84	67.747	31.906	27.854	1.00	43.83
ATOM	660	CA	THR	84	67.111	33.099	27.311	1.00	43.71
ATOM	661	CB	THR	84	65.603	33.090	27.582	1.00	43.70
ATOM	662	OG1	THR	84	64.976	32.119	26.732	1.00	44.53
ATOM	663	CG2	THR	84	64.997	34.446	27.312	1.00	46.08
ATOM	664	C	THR	84	67.748	34.291	27.999	1.00	45.07
ATOM	665	O	THR	84	67.577	35.433	27.590	1.00	45.57
ATOM	666	N	GLN	85	68.499	33.999	29.053	1.00	46.19
ATOM	667	CA	GLN	85	69.202	35.009	29.827	1.00	47.00

ATOM	668	CB	GLN	85	68.398	35.387	31.064	1.00	48.71
ATOM	669	CG	GLN	85	67.018	35.903	30.776	1.00	54.49
ATOM	670	CD	GLN	85	66.134	35.842	32.007	1.00	59.66
ATOM	671	OE1	GLN	85	66.463	36.415	33.053	1.00	59.91
ATOM	672	NE2	GLN	85	65.005	35.138	31.893	1.00	60.96
ATOM	673	C	GLN	85	70.497	34.343	30.249	1.00	46.30
ATOM	674	O	GLN	85	70.515	33.135	30.496	1.00	45.05
ATOM	675	N	LEU	86	71.575	35.113	30.350	1.00	44.87
ATOM	676	CA	LEU	86	72.850	34.522	30.724	1.00	44.82
ATOM	677	CB	LEU	86	73.803	34.532	29.535	1.00	42.60
ATOM	678	CG	LEU	86	73.321	33.774	28.304	1.00	44.41
ATOM	679	CD1	LEU	86	74.329	33.988	27.186	1.00	47.40
ATOM	680	CD2	LEU	86	73.161	32.287	28.620	1.00	42.93
ATOM	681	C	LEU	86	73.523	35.216	31.879	1.00	45.57
ATOM	682	O	LEU	86	73.408	36.429	32.045	1.00	48.26
ATOM	683	N	PHE	87	74.225	34.434	32.683	1.00	43.87
ATOM	684	CA	PHE	87	74.959	34.987	33.800	1.00	43.63
ATOM	685	CB	PHE	87	75.444	33.853	34.689	1.00	40.78
ATOM	686	CG	PHE	87	76.231	34.313	35.857	1.00	40.85
ATOM	687	CD1	PHE	87	75.626	35.038	36.869	1.00	40.47
ATOM	688	CD2	PHE	87	77.586	34.037	35.946	1.00	41.63
ATOM	689	CE1	PHE	87	76.362	35.481	37.955	1.00	41.04
ATOM	690	CE2	PHE	87	78.332	34.476	37.031	1.00	40.73
ATOM	691	CZ	PHE	87	77.719	35.200	38.037	1.00	40.21
ATOM	692	C	PHE	87	76.143	35.729	33.154	1.00	45.18
ATOM	693	O	PHE	87	76.785	35.199	32.244	1.00	44.05
ATOM	694	N	GLU	88	76.420	36.951	33.610	1.00	46.88
ATOM	695	CA	GLU	88	77.496	37.769	33.046	1.00	50.12
ATOM	696	CB	GLU	88	78.869	37.225	33.436	1.00	50.94
ATOM	697	CG	GLU	88	79.183	37.333	34.915	1.00	54.47
ATOM	698	CD	GLU	88	80.582	36.842	35.252	1.00	56.68
ATOM	699	OE1	GLU	88	80.903	36.719	36.461	1.00	58.66
ATOM	700	OE2	GLU	88	81.363	36.584	34.308	1.00	56.70
ATOM	701	C	GLU	88	77.398	37.837	31.524	1.00	52.26
ATOM	702	O	GLU	88	78.383	38.105	30.838	1.00	53.70
ATOM	703	N	ASP	89	76.205	37.575	31.004	1.00	53.97
ATOM	704	CA	ASP	89	75.954	37.622	29.566	1.00	55.67
ATOM	705	CB	ASP	89	76.369	38.988	29.012	1.00	56.99
ATOM	706	CG	ASP	89	75.403	40.082	29.404	1.00	59.00
ATOM	707	OD1	ASP	89	74.189	39.894	29.157	1.00	60.54
ATOM	708	OD2	ASP	89	75.850	41.115	29.956	1.00	56.93
ATOM	709	C	ASP	89	76.579	36.527	28.706	1.00	54.74
ATOM	710	O	ASP	89	76.530	36.604	27.478	1.00	55.07
ATOM	711	N	ASN	90	77.143	35.497	29.325	1.00	54.15
ATOM	712	CA	ASN	90	77.764	34.438	28.538	1.00	52.57
ATOM	713	CB	ASN	90	79.277	34.595	28.584	1.00	52.47
ATOM	714	CG	ASN	90	79.737	35.890	27.980	1.00	53.25
ATOM	715	OD1	ASN	90	79.531	36.135	26.794	1.00	54.48
ATOM	716	ND2	ASN	90	80.359	36.736	28.791	1.00	52.67
ATOM	717	C	ASN	90	77.426	33.015	28.949	1.00	51.81
ATOM	718	O	ASN	90	77.363	32.115	28.114	1.00	51.39
ATOM	719	N	TYR	91	77.187	32.803	30.231	1.00	50.25
ATOM	720	CA	TYR	91	76.949	31.453	30.677	1.00	49.51
ATOM	721	CB	TYR	91	77.887	31.174	31.845	1.00	51.13
ATOM	722	CG	TYR	91	79.291	31.674	31.567	1.00	52.63
ATOM	723	CD1	TYR	91	79.699	32.943	31.984	1.00	53.04
ATOM	724	CE1	TYR	91	80.979	33.427	31.696	1.00	53.62
ATOM	725	CD2	TYR	91	80.202	30.893	30.851	1.00	54.91
ATOM	726	CE2	TYR	91	81.489	31.368	30.554	1.00	55.55
ATOM	727	CZ	TYR	91	81.869	32.634	30.981	1.00	55.51
ATOM	728	OH	TYR	91	83.136	33.101	30.703	1.00	54.62

ATOM	729	C	TYR	91	75.535	31.020	31.013	1.00	47.39
ATOM	730	O	TYR	91	74.803	31.713	31.719	1.00	47.32
ATOM	731	N	ALA	92	75.161	29.864	30.471	1.00	44.48
ATOM	732	CA	ALA	92	73.863	29.281	30.730	1.00	43.50
ATOM	733	CB	ALA	92	73.474	28.356	29.613	1.00	40.46
ATOM	734	C	ALA	92	74.012	28.499	32.030	1.00	44.42
ATOM	735	O	ALA	92	73.025	28.223	32.716	1.00	46.43
ATOM	736	N	LEU	93	75.252	28.136	32.359	1.00	42.65
ATOM	737	CA	LEU	93	75.539	27.395	33.583	1.00	41.17
ATOM	738	CB	LEU	93	75.734	25.917	33.284	1.00	38.62
ATOM	739	CG	LEU	93	76.143	25.090	34.505	1.00	37.50
ATOM	740	CD1	LEU	93	75.067	25.170	35.582	1.00	38.29
ATOM	741	CD2	LEU	93	76.360	23.652	34.087	1.00	36.61
ATOM	742	C	LEU	93	76.776	27.934	34.298	1.00	41.94
ATOM	743	O	LEU	93	77.865	27.986	33.730	1.00	42.96
ATOM	744	N	ALA	94	76.599	28.325	35.554	1.00	40.94
ATOM	745	CA	ALA	94	77.686	28.878	36.335	1.00	41.22
ATOM	746	CB	ALA	94	77.506	30.378	36.461	1.00	39.61
ATOM	747	C	ALA	94	77.766	28.241	37.720	1.00	43.35
ATOM	748	O	ALA	94	76.814	28.299	38.499	1.00	42.96
ATOM	749	N	VAL	95	78.911	27.632	38.017	1.00	44.35
ATOM	750	CA	VAL	95	79.143	26.996	39.307	1.00	45.11
ATOM	751	CB	VAL	95	79.388	25.500	39.125	1.00	43.05
ATOM	752	CG1	VAL	95	79.533	24.819	40.479	1.00	39.27
ATOM	753	CG2	VAL	95	78.240	24.899	38.312	1.00	40.86
ATOM	754	C	VAL	95	80.369	27.669	39.925	1.00	48.52
ATOM	755	O	VAL	95	81.508	27.415	39.517	1.00	48.34
ATOM	756	N	LEU	96	80.128	28.524	40.916	1.00	50.32
ATOM	757	CA	LEU	96	81.207	29.272	41.542	1.00	51.50
ATOM	758	CB	LEU	96	81.074	30.739	41.150	1.00	51.70
ATOM	759	CG	LEU	96	80.684	30.959	39.690	1.00	52.86
ATOM	760	CD1	LEU	96	80.346	32.418	39.457	1.00	52.63
ATOM	761	CD2	LEU	96	81.821	30.512	38.793	1.00	53.82
ATOM	762	C	LEU	96	81.323	29.181	43.059	1.00	53.24
ATOM	763	O	LEU	96	80.344	28.970	43.774	1.00	53.15
ATOM	764	N	ASP	97	82.555	29.359	43.524	1.00	54.82
ATOM	765	CA	ASP	97	82.906	29.347	44.938	1.00	55.39
ATOM	766	CB	ASP	97	82.927	30.780	45.456	1.00	53.38
ATOM	767	CG	ASP	97	83.658	31.711	44.521	1.00	53.93
ATOM	768	OD1	ASP	97	83.020	32.242	43.586	1.00	52.94
ATOM	769	OD2	ASP	97	84.879	31.892	44.706	1.00	53.79
ATOM	770	C	ASP	97	82.055	28.476	45.850	1.00	57.18
ATOM	771	O	ASP	97	81.505	28.948	46.849	1.00	55.28
ATOM	772	N	ASN	98	81.962	27.197	45.510	1.00	59.71
ATOM	773	CA	ASN	98	81.208	26.253	46.318	1.00	63.26
ATOM	774	CB	ASN	98	80.327	25.394	45.421	1.00	61.80
ATOM	775	CG	ASN	98	79.265	26.203	44.735	1.00	60.81
ATOM	776	OD1	ASN	98	78.351	26.712	45.383	1.00	62.45
ATOM	777	ND2	ASN	98	79.382	26.350	43.419	1.00	59.92
ATOM	778	C	ASN	98	82.186	25.391	47.108	1.00	65.67
ATOM	779	O	ASN	98	82.574	24.313	46.673	1.00	65.42
ATOM	780	N	GLY	99	82.579	25.894	48.272	1.00	70.08
ATOM	781	CA	GLY	99	83.520	25.197	49.125	1.00	76.22
ATOM	782	C	GLY	99	84.105	26.187	50.116	1.00	81.42
ATOM	783	O	GLY	99	84.487	27.299	49.740	1.00	81.92
ATOM	784	N	ASP	100	84.176	25.774	51.374	1.00	86.13
ATOM	785	CA	ASP	100	84.686	26.590	52.475	1.00	90.98
ATOM	786	CB	ASP	100	85.046	25.680	53.656	1.00	92.47
ATOM	787	CG	ASP	100	83.883	24.805	54.092	1.00	94.56
ATOM	788	OD1	ASP	100	82.875	25.358	54.582	1.00	96.09
ATOM	789	OD2	ASP	100	83.973	23.566	53.941	1.00	94.94

ATOM	790	C	ASP	100	85.861	27.531	52.179	1.00	93.79
ATOM	791	O	ASP	100	85.739	28.743	52.365	1.00	93.83
ATOM	792	N	PRO	101	87.015	26.998	51.735	1.00	96.96
ATOM	793	CD	PRO	101	87.480	25.609	51.851	1.00	98.24
ATOM	794	CA	PRO	101	88.159	27.878	51.444	1.00	99.43
ATOM	795	CB	PRO	101	89.366	26.938	51.564	1.00	98.97
ATOM	796	CG	PRO	101	88.860	25.813	52.424	1.00	99.32
ATOM	797	C	PRO	101	88.097	28.543	50.071	1.00	101.35
ATOM	798	O	PRO	101	87.014	28.846	49.567	1.00	102.76
ATOM	799	N	LEU	102	89.270	28.769	49.477	1.00	102.83
ATOM	800	CA	LEU	102	89.374	29.398	48.156	1.00	104.27
ATOM	801	CB	LEU	102	89.462	30.925	48.291	1.00	104.27
ATOM	802	CG	LEU	102	89.534	31.548	47.017	1.00	103.47
ATOM	803	C	LEU	102	90.587	28.889	47.369	1.00	104.76
ATOM	804	O	LEU	102	91.737	29.157	47.724	1.00	104.83
ATOM	805	N	PRO	107	90.748	18.959	64.154	1.00	126.18
ATOM	806	CA	PRO	107	89.727	17.932	63.974	1.00	126.66
ATOM	807	CB	PRO	107	88.542	18.209	64.898	1.00	126.29
ATOM	808	C	PRO	107	89.260	17.878	62.517	1.00	126.87
ATOM	809	O	PRO	107	88.076	18.060	62.223	1.00	127.11
ATOM	810	N	VAL	108	90.202	17.618	61.613	1.00	126.89
ATOM	811	CA	VAL	108	89.916	17.548	60.181	1.00	126.48
ATOM	812	CB	VAL	108	91.231	17.551	59.391	1.00	126.25
ATOM	813	C	VAL	108	89.074	16.331	59.790	1.00	125.86
ATOM	814	O	VAL	108	87.889	16.464	59.470	1.00	125.34
ATOM	815	N	THR	109	89.698	15.154	59.819	1.00	125.17
ATOM	816	CA	THR	109	89.049	13.890	59.461	1.00	123.95
ATOM	817	CB	THR	109	89.792	12.719	60.113	1.00	124.08
ATOM	818	C	THR	109	87.566	13.828	59.824	1.00	122.63
ATOM	819	O	THR	109	86.754	13.313	59.050	1.00	122.80
ATOM	820	N	GLY	110	87.224	14.351	60.999	1.00	120.61
ATOM	821	CA	GLY	110	85.844	14.343	61.449	1.00	117.57
ATOM	822	C	GLY	110	84.853	14.918	60.453	1.00	115.50
ATOM	823	O	GLY	110	84.260	14.183	59.659	1.00	116.01
ATOM	824	N	ALA	111	84.673	16.234	60.490	1.00	112.70
ATOM	825	CA	ALA	111	83.734	16.913	59.600	1.00	109.22
ATOM	826	CB	ALA	111	83.549	18.363	60.053	1.00	109.74
ATOM	827	C	ALA	111	84.146	16.876	58.127	1.00	106.68
ATOM	828	O	ALA	111	85.218	17.366	57.754	1.00	106.45
ATOM	829	N	SER	112	83.285	16.294	57.293	1.00	103.09
ATOM	830	CA	SER	112	83.538	16.211	55.858	1.00	99.27
ATOM	831	CB	SER	112	82.483	15.337	55.175	1.00	99.51
ATOM	832	OG	SER	112	82.457	14.037	55.735	1.00	101.30
ATOM	833	C	SER	112	83.476	17.622	55.285	1.00	96.09
ATOM	834	O	SER	112	82.460	18.310	55.408	1.00	96.48
ATOM	835	N	PRO	113	84.564	18.071	54.644	1.00	92.15
ATOM	836	CD	PRO	113	85.785	17.320	54.307	1.00	91.00
ATOM	837	CA	PRO	113	84.601	19.415	54.061	1.00	88.77
ATOM	838	CB	PRO	113	85.804	19.344	53.123	1.00	89.27
ATOM	839	CG	PRO	113	86.720	18.417	53.848	1.00	90.34
ATOM	840	C	PRO	113	83.309	19.782	53.333	1.00	84.95
ATOM	841	O	PRO	113	82.662	18.929	52.720	1.00	84.81
ATOM	842	N	GLY	114	82.930	21.052	53.422	1.00	80.54
ATOM	843	CA	GLY	114	81.729	21.506	52.754	1.00	75.55
ATOM	844	C	GLY	114	82.044	21.832	51.310	1.00	72.23
ATOM	845	O	GLY	114	83.199	22.076	50.961	1.00	71.35
ATOM	846	N	GLY	115	81.021	21.834	50.465	1.00	69.91
ATOM	847	CA	GLY	115	81.232	22.137	49.061	1.00	66.25
ATOM	848	C	GLY	115	80.635	21.080	48.157	1.00	63.68
ATOM	849	O	GLY	115	80.481	19.926	48.557	1.00	62.37
ATOM	850	N	LEU	116	80.292	21.484	46.937	1.00	62.02

ATOM	851	CA	LEU	116	79.709	20.582	45.948	1.00	59.67
ATOM	852	CB	LEU	116	79.271	21.387	44.723	1.00	57.68
ATOM	853	CG	LEU	116	78.388	20.692	43.691	1.00	56.19
ATOM	854	CD1	LEU	116	77.022	20.411	44.296	1.00	54.53
ATOM	855	CD2	LEU	116	78.261	21.582	42.456	1.00	56.83
ATOM	856	C	LEU	116	80.764	19.544	45.551	1.00	59.55
ATOM	857	O	LEU	116	81.900	19.901	45.220	1.00	58.10
ATOM	858	N	ARG	117	80.390	18.267	45.587	1.00	59.24
ATOM	859	CA	ARG	117	81.327	17.195	45.253	1.00	59.70
ATOM	860	CB	ARG	117	81.109	15.992	46.174	1.00	60.56
ATOM	861	CG	ARG	117	81.021	16.374	47.632	1.00	62.94
ATOM	862	CD	ARG	117	81.319	15.216	48.560	1.00	67.09
ATOM	863	NE	ARG	117	82.602	15.403	49.230	1.00	72.49
ATOM	864	CZ	ARG	117	82.917	16.462	49.975	1.00	75.62
ATOM	865	NH1	ARG	117	82.042	17.447	50.157	1.00	76.20
ATOM	866	NH2	ARG	117	84.118	16.545	50.530	1.00	76.65
ATOM	867	C	ARG	117	81.209	16.765	43.798	1.00	58.65
ATOM	868	O	ARG	117	82.219	16.549	43.121	1.00	58.41
ATOM	869	N	GLU	118	79.972	16.644	43.326	1.00	57.45
ATOM	870	CA	GLU	118	79.703	16.264	41.946	1.00	56.49
ATOM	871	CB	GLU	118	79.584	14.737	41.840	1.00	56.46
ATOM	872	CG	GLU	118	78.782	14.074	42.940	1.00	57.68
ATOM	873	CD	GLU	118	78.794	12.550	42.845	1.00	58.93
ATOM	874	OE1	GLU	118	79.886	11.944	42.929	1.00	59.44
ATOM	875	OE2	GLU	118	77.709	11.951	42.689	1.00	59.58
ATOM	876	C	GLU	118	78.442	16.959	41.423	1.00	55.19
ATOM	877	O	GLU	118	77.498	17.192	42.176	1.00	57.56
ATOM	878	N	LEU	119	78.432	17.304	40.139	1.00	52.98
ATOM	879	CA	LEU	119	77.283	17.983	39.536	1.00	50.77
ATOM	880	CB	LEU	119	77.689	18.563	38.184	1.00	47.76
ATOM	881	CG	LEU	119	78.554	19.824	38.302	1.00	45.09
ATOM	882	CD1	LEU	119	79.187	20.143	36.971	1.00	43.63
ATOM	883	CD2	LEU	119	77.704	20.989	38.787	1.00	41.01
ATOM	884	C	LEU	119	76.038	17.103	39.391	1.00	51.28
ATOM	885	O	LEU	119	74.925	17.532	39.676	1.00	50.10
ATOM	886	N	GLN	120	76.220	15.872	38.941	1.00	53.25
ATOM	887	CA	GLN	120	75.100	14.944	38.815	1.00	56.61
ATOM	888	CB	GLN	120	74.588	14.560	40.210	1.00	60.68
ATOM	889	CG	GLN	120	75.660	13.965	41.121	1.00	64.56
ATOM	890	CD	GLN	120	75.098	12.947	42.109	1.00	68.65
ATOM	891	OE1	GLN	120	74.466	11.961	41.711	1.00	70.06
ATOM	892	NE2	GLN	120	75.337	13.174	43.402	1.00	69.09
ATOM	893	C	GLN	120	73.921	15.404	37.951	1.00	56.07
ATOM	894	O	GLN	120	72.769	15.038	38.207	1.00	56.45
ATOM	895	N	LEU	121	74.220	16.197	36.927	1.00	55.01
ATOM	896	CA	LEU	121	73.213	16.687	35.987	1.00	53.16
ATOM	897	CB	LEU	121	73.667	18.017	35.383	1.00	52.15
ATOM	898	CG	LEU	121	73.852	19.173	36.360	1.00	51.71
ATOM	899	CD1	LEU	121	74.598	20.300	35.673	1.00	49.86
ATOM	900	CD2	LEU	121	72.485	19.632	36.868	1.00	50.80
ATOM	901	C	LEU	121	73.154	15.636	34.890	1.00	52.58
ATOM	902	O	LEU	121	73.450	15.919	33.729	1.00	53.15
ATOM	903	N	ARG	122	72.765	14.422	35.253	1.00	52.13
ATOM	904	CA	ARG	122	72.741	13.336	34.288	1.00	51.57
ATOM	905	CB	ARG	122	72.730	12.005	35.029	1.00	53.46
ATOM	906	CG	ARG	122	71.586	11.827	35.995	1.00	55.67
ATOM	907	CD	ARG	122	72.026	10.906	37.111	1.00	58.36
ATOM	908	NE	ARG	122	70.896	10.320	37.815	1.00	62.96
ATOM	909	CZ	ARG	122	70.976	9.795	39.032	1.00	65.49
ATOM	910	NH1	ARG	122	72.140	9.790	39.680	1.00	64.20
ATOM	911	NH2	ARG	122	69.891	9.273	39.596	1.00	67.00

ATOM	912	C	ARG	122	71.656	13.358	33.222	1.00	49.90
ATOM	913	O	ARG	122	71.640	12.504	32.333	1.00	50.83
ATOM	914	N	SER	123	70.756	14.330	33.292	1.00	46.61
ATOM	915	CA	SER	123	69.701	14.434	32.293	1.00	42.82
ATOM	916	CB	SER	123	68.335	14.530	32.967	1.00	42.47
ATOM	917	OG	SER	123	68.038	13.341	33.670	1.00	38.70
ATOM	918	C	SER	123	69.934	15.663	31.430	1.00	41.29
ATOM	919	O	SER	123	69.282	15.850	30.407	1.00	40.43
ATOM	920	N	LEU	124	70.879	16.496	31.849	1.00	40.71
ATOM	921	CA	LEU	124	71.187	17.715	31.119	1.00	40.84
ATOM	922	CB	LEU	124	72.055	18.649	31.956	1.00	37.35
ATOM	923	CG	LEU	124	72.435	19.929	31.211	1.00	37.32
ATOM	924	CD1	LEU	124	71.166	20.651	30.771	1.00	35.84
ATOM	925	CD2	LEU	124	73.291	20.821	32.089	1.00	35.21
ATOM	926	C	LEU	124	71.888	17.428	29.809	1.00	43.38
ATOM	927	O	LEU	124	73.109	17.252	29.769	1.00	43.33
ATOM	928	N	THR	125	71.104	17.407	28.733	1.00	45.11
ATOM	929	CA	THR	125	71.621	17.138	27.397	1.00	43.33
ATOM	930	CB	THR	125	70.913	15.918	26.783	1.00	43.30
ATOM	931	OG1	THR	125	69.496	16.104	26.878	1.00	42.09
ATOM	932	CG2	THR	125	71.305	14.639	27.510	1.00	39.71
ATOM	933	C	THR	125	71.409	18.319	26.456	1.00	43.96
ATOM	934	O	THR	125	71.624	18.198	25.253	1.00	44.38
ATOM	935	N	GLU	126	70.994	19.465	26.986	1.00	43.81
ATOM	936	CA	GLU	126	70.745	20.598	26.106	1.00	42.67
ATOM	937	CB	GLU	126	69.350	20.470	25.500	1.00	41.42
ATOM	938	CG	GLU	126	69.020	21.521	24.453	1.00	41.40
ATOM	939	CD	GLU	126	69.512	21.153	23.061	1.00	43.48
ATOM	940	OE1	GLU	126	68.830	20.358	22.370	1.00	41.80
ATOM	941	OE2	GLU	126	70.587	21.658	22.661	1.00	42.13
ATOM	942	C	GLU	126	70.879	21.990	26.709	1.00	43.68
ATOM	943	O	GLU	126	70.234	22.317	27.704	1.00	45.80
ATOM	944	N	ILE	127	71.736	22.798	26.094	1.00	42.47
ATOM	945	CA	ILE	127	71.933	24.192	26.479	1.00	41.14
ATOM	946	CB	ILE	127	73.318	24.426	27.085	1.00	38.54
ATOM	947	CG2	ILE	127	73.574	25.911	27.245	1.00	33.94
ATOM	948	CG1	ILE	127	73.406	23.722	28.437	1.00	36.30
ATOM	949	CD1	ILE	127	74.784	23.818	29.093	1.00	36.27
ATOM	950	C	ILE	127	71.790	24.944	25.149	1.00	43.31
ATOM	951	O	ILE	127	72.715	24.974	24.325	1.00	42.28
ATOM	952	N	LEU	128	70.609	25.523	24.935	1.00	44.48
ATOM	953	CA	LEU	128	70.312	26.222	23.690	1.00	44.79
ATOM	954	CB	LEU	128	68.851	26.661	23.678	1.00	44.23
ATOM	955	CG	LEU	128	67.875	25.475	23.692	1.00	45.11
ATOM	956	CD1	LEU	128	66.427	25.981	23.643	1.00	41.10
ATOM	957	CD2	LEU	128	68.183	24.555	22.499	1.00	41.18
ATOM	958	C	LEU	128	71.203	27.400	23.376	1.00	45.64
ATOM	959	O	LEU	128	71.668	27.543	22.247	1.00	47.14
ATOM	960	N	LYS	129	71.454	28.232	24.378	1.00	45.50
ATOM	961	CA	LYS	129	72.283	29.415	24.201	1.00	45.15
ATOM	962	CB	LYS	129	71.368	30.629	23.983	1.00	47.19
ATOM	963	CG	LYS	129	72.057	31.989	23.869	1.00	51.77
ATOM	964	CD	LYS	129	71.021	33.124	23.825	1.00	53.80
ATOM	965	CE	LYS	129	71.666	34.507	23.978	1.00	56.48
ATOM	966	NZ	LYS	129	70.669	35.618	24.130	1.00	55.90
ATOM	967	C	LYS	129	73.143	29.607	25.447	1.00	44.99
ATOM	968	O	LYS	129	72.694	29.343	26.559	1.00	44.46
ATOM	969	N	GLY	130	74.384	30.049	25.267	1.00	45.43
ATOM	970	CA	GLY	130	75.240	30.275	26.422	1.00	45.56
ATOM	971	C	GLY	130	76.270	29.201	26.713	1.00	45.03
ATOM	972	O	GLY	130	76.214	28.104	26.161	1.00	44.57

ATOM	973	N	GLY	131	77.205	29.519	27.605	1.00	44.82
ATOM	974	CA	GLY	131	78.261	28.581	27.934	1.00	46.22
ATOM	975	C	GLY	131	78.315	28.070	29.361	1.00	45.93
ATOM	976	O	GLY	131	77.367	28.197	30.126	1.00	47.97
ATOM	977	N	VAL	132	79.449	27.493	29.724	1.00	45.40
ATOM	978	CA	VAL	132	79.615	26.936	31.050	1.00	45.70
ATOM	979	CB	VAL	132	79.794	25.405	30.980	1.00	44.20
ATOM	980	CG1	VAL	132	80.046	24.846	32.360	1.00	43.09
ATOM	981	CG2	VAL	132	78.549	24.768	30.366	1.00	45.15
ATOM	982	C	VAL	132	80.804	27.534	31.777	1.00	47.30
ATOM	983	O	VAL	132	81.938	27.507	31.282	1.00	47.68
ATOM	984	N	LEU	133	80.524	28.071	32.961	1.00	47.58
ATOM	985	CA	LEU	133	81.535	28.675	33.807	1.00	47.58
ATOM	986	CB	LEU	133	81.189	30.136	34.095	1.00	47.73
ATOM	987	CG	LEU	133	82.080	30.807	35.148	1.00	49.20
ATOM	988	CD1	LEU	133	83.501	30.936	34.599	1.00	47.21
ATOM	989	CD2	LEU	133	81.509	32.171	35.525	1.00	46.27
ATOM	990	C	LEU	133	81.590	27.902	35.120	1.00	48.57
ATOM	991	O	LEU	133	80.625	27.889	35.888	1.00	48.62
ATOM	992	N	ILE	134	82.715	27.246	35.369	1.00	47.15
ATOM	993	CA	ILE	134	82.876	26.496	36.599	1.00	47.05
ATOM	994	CB	ILE	134	82.847	24.974	36.328	1.00	43.42
ATOM	995	CG2	ILE	134	82.963	24.210	37.633	1.00	41.94
ATOM	996	CG1	ILE	134	81.537	24.603	35.622	1.00	42.18
ATOM	997	CD1	ILE	134	81.321	23.115	35.409	1.00	36.15
ATOM	998	C	ILE	134	84.205	26.916	37.221	1.00	48.77
ATOM	999	O	ILE	134	85.273	26.640	36.673	1.00	49.10
ATOM	1000	N	GLN	135	84.130	27.594	38.363	1.00	49.58
ATOM	1001	CA	GLN	135	85.326	28.080	39.040	1.00	50.96
ATOM	1002	CB	GLN	135	85.527	29.572	38.738	1.00	51.43
ATOM	1003	CG	GLN	135	85.562	29.950	37.267	1.00	54.23
ATOM	1004	CD	GLN	135	86.913	29.700	36.610	1.00	56.24
ATOM	1005	OE1	GLN	135	87.910	30.347	36.939	1.00	58.47
ATOM	1006	NE2	GLN	135	86.948	28.761	35.670	1.00	57.30
ATOM	1007	C	GLN	135	85.286	27.904	40.557	1.00	51.50
ATOM	1008	O	GLN	135	84.223	27.833	41.172	1.00	53.24
ATOM	1009	N	ARG	136	86.472	27.840	41.146	1.00	51.51
ATOM	1010	CA	ARG	136	86.641	27.734	42.588	1.00	49.89
ATOM	1011	CB	ARG	136	86.613	29.149	43.175	1.00	48.50
ATOM	1012	CG	ARG	136	87.537	30.115	42.420	1.00	47.11
ATOM	1013	CD	ARG	136	87.473	31.547	42.951	1.00	47.61
ATOM	1014	NE	ARG	136	86.249	32.246	42.566	1.00	48.00
ATOM	1015	CZ	ARG	136	85.970	32.657	41.331	1.00	49.03
ATOM	1016	NH1	ARG	136	86.826	32.447	40.338	1.00	48.98
ATOM	1017	NH2	ARG	136	84.825	33.280	41.087	1.00	48.99
ATOM	1018	C	ARG	136	85.680	26.814	43.344	1.00	49.80
ATOM	1019	O	ARG	136	84.969	27.239	44.255	1.00	49.62
ATOM	1020	N	ASN	137	85.681	25.542	42.965	1.00	50.11
ATOM	1021	CA	ASN	137	84.852	24.531	43.614	1.00	51.52
ATOM	1022	CB	ASN	137	83.836	23.984	42.619	1.00	49.76
ATOM	1023	CG	ASN	137	82.946	25.068	42.071	1.00	47.43
ATOM	1024	OD1	ASN	137	82.109	25.615	42.792	1.00	47.56
ATOM	1025	ND2	ASN	137	83.138	25.411	40.800	1.00	44.58
ATOM	1026	C	ASN	137	85.791	23.425	44.098	1.00	53.46
ATOM	1027	O	ASN	137	86.001	22.417	43.416	1.00	54.02
ATOM	1028	N	PRO	138	86.378	23.620	45.291	1.00	54.39
ATOM	1029	CD	PRO	138	86.090	24.835	46.069	1.00	54.92
ATOM	1030	CA	PRO	138	87.324	22.770	46.023	1.00	55.10
ATOM	1031	CB	PRO	138	87.391	23.445	47.388	1.00	56.13
ATOM	1032	CG	PRO	138	87.246	24.875	47.030	1.00	55.77
ATOM	1033	C	PRO	138	87.057	21.267	46.141	1.00	54.62

ATOM	1034	O	PRO	138	87.997	20.474	46.095	1.00	55.62
ATOM	1035	N	GLN	139	85.798	20.873	46.309	1.00	52.71
ATOM	1036	CA	GLN	139	85.470	19.457	46.445	1.00	50.41
ATOM	1037	CB	GLN	139	84.503	19.245	47.600	1.00	54.28
ATOM	1038	CG	GLN	139	84.965	19.780	48.927	1.00	57.44
ATOM	1039	CD	GLN	139	86.251	19.143	49.366	1.00	60.16
ATOM	1040	OE1	GLN	139	86.410	17.920	49.286	1.00	59.39
ATOM	1041	NE2	GLN	139	87.183	19.964	49.843	1.00	61.11
ATOM	1042	C	GLN	139	84.812	18.881	45.212	1.00	48.99
ATOM	1043	O	GLN	139	84.227	17.806	45.291	1.00	49.44
ATOM	1044	N	LEU	140	84.910	19.573	44.080	1.00	46.61
ATOM	1045	CA	LEU	140	84.249	19.127	42.851	1.00	45.80
ATOM	1046	CB	LEU	140	83.748	20.353	42.079	1.00	42.36
ATOM	1047	CG	LEU	140	82.885	20.080	40.845	1.00	38.55
ATOM	1048	CD1	LEU	140	81.566	19.439	41.262	1.00	36.83
ATOM	1049	CD2	LEU	140	82.638	21.376	40.108	1.00	36.26
ATOM	1050	C	LEU	140	85.024	18.220	41.887	1.00	48.03
ATOM	1051	O	LEU	140	86.151	18.521	41.491	1.00	48.11
ATOM	1052	N	CYS	141	84.387	17.120	41.487	1.00	49.94
ATOM	1053	CA	CYS	141	84.983	16.165	40.553	1.00	51.42
ATOM	1054	C	CYS	141	84.155	15.955	39.281	1.00	52.28
ATOM	1055	O	CYS	141	82.986	16.342	39.201	1.00	52.04
ATOM	1056	CB	CYS	141	85.161	14.804	41.227	1.00	53.37
ATOM	1057	SG	CYS	141	86.472	14.727	42.484	1.00	55.47
ATOM	1058	N	TYR	142	84.790	15.342	38.288	1.00	52.23
ATOM	1059	CA	TYR	142	84.153	14.988	37.024	1.00	53.02
ATOM	1060	CB	TYR	142	82.922	14.114	37.307	1.00	55.55
ATOM	1061	CG	TYR	142	83.220	13.021	38.306	1.00	57.71
ATOM	1062	CD1	TYR	142	82.807	13.131	39.633	1.00	58.55
ATOM	1063	CE1	TYR	142	83.154	12.162	40.580	1.00	60.12
ATOM	1064	CD2	TYR	142	83.986	11.911	37.944	1.00	59.09
ATOM	1065	CE2	TYR	142	84.340	10.937	38.882	1.00	59.55
ATOM	1066	CZ	TYR	142	83.922	11.069	40.197	1.00	60.59
ATOM	1067	OH	TYR	142	84.281	10.119	41.130	1.00	61.97
ATOM	1068	C	TYR	142	83.777	16.077	36.038	1.00	52.13
ATOM	1069	O	TYR	142	83.566	15.787	34.862	1.00	52.66
ATOM	1070	N	GLN	143	83.696	17.323	36.484	1.00	51.73
ATOM	1071	CA	GLN	143	83.326	18.392	35.563	1.00	51.08
ATOM	1072	CB	GLN	143	83.391	19.754	36.259	1.00	48.67
ATOM	1073	CG	GLN	143	84.799	20.275	36.459	1.00	47.89
ATOM	1074	CD	GLN	143	85.361	19.948	37.822	1.00	47.25
ATOM	1075	OE1	GLN	143	85.186	18.839	38.337	1.00	46.97
ATOM	1076	NE2	GLN	143	86.056	20.913	38.415	1.00	45.50
ATOM	1077	C	GLN	143	84.213	18.426	34.310	1.00	51.56
ATOM	1078	O	GLN	143	83.800	18.931	33.267	1.00	50.46
ATOM	1079	N	ASP	144	85.427	17.889	34.414	1.00	53.39
ATOM	1080	CA	ASP	144	86.362	17.888	33.284	1.00	54.95
ATOM	1081	CB	ASP	144	87.806	18.001	33.795	1.00	57.46
ATOM	1082	CG	ASP	144	88.158	16.928	34.823	1.00	60.87
ATOM	1083	OD1	ASP	144	87.240	16.420	35.508	1.00	61.77
ATOM	1084	OD2	ASP	144	89.361	16.605	34.956	1.00	61.23
ATOM	1085	C	ASP	144	86.227	16.698	32.336	1.00	54.14
ATOM	1086	O	ASP	144	86.718	16.746	31.211	1.00	54.76
ATOM	1087	N	THR	145	85.548	15.644	32.779	1.00	52.72
ATOM	1088	CA	THR	145	85.344	14.456	31.954	1.00	51.50
ATOM	1089	CB	THR	145	85.184	13.194	32.806	1.00	52.77
ATOM	1090	OG1	THR	145	83.810	13.078	33.220	1.00	53.52
ATOM	1091	CG2	THR	145	86.095	13.250	34.025	1.00	50.79
ATOM	1092	C	THR	145	84.072	14.547	31.114	1.00	51.38
ATOM	1093	O	THR	145	83.705	13.593	30.428	1.00	51.92
ATOM	1094	N	ILE	146	83.386	15.682	31.180	1.00	51.88

ATOM	1095	CA	ILE	146	82.136	15.856	30.444	1.00	49.69
ATOM	1096	CB	ILE	146	81.122	16.710	31.258	1.00	49.09
ATOM	1097	CG2	ILE	146	79.967	17.145	30.367	1.00	48.38
ATOM	1098	CG1	ILE	146	80.609	15.914	32.467	1.00	48.35
ATOM	1099	CD1	ILE	146	79.764	14.689	32.112	1.00	47.73
ATOM	1100	C	ILE	146	82.349	16.511	29.093	1.00	49.10
ATOM	1101	O	ILE	146	83.057	17.515	28.982	1.00	49.69
ATOM	1102	N	LEU	147	81.739	15.942	28.061	1.00	47.61
ATOM	1103	CA	LEU	147	81.864	16.512	26.735	1.00	46.57
ATOM	1104	CB	LEU	147	81.662	15.435	25.669	1.00	46.78
ATOM	1105	CG	LEU	147	81.972	15.868	24.228	1.00	48.10
ATOM	1106	CD1	LEU	147	83.424	16.331	24.128	1.00	44.45
ATOM	1107	CD2	LEU	147	81.706	14.709	23.274	1.00	46.61
ATOM	1108	C	LEU	147	80.793	17.589	26.617	1.00	47.11
ATOM	1109	O	LEU	147	79.653	17.317	26.230	1.00	47.80
ATOM	1110	N	TRP	148	81.163	18.815	26.966	1.00	47.15
ATOM	1111	CA	TRP	148	80.231	19.940	26.920	1.00	48.80
ATOM	1112	CB	TRP	148	80.876	21.170	27.571	1.00	49.02
ATOM	1113	CG	TRP	148	81.187	20.945	29.021	1.00	48.42
ATOM	1114	CD2	TRP	148	80.251	20.955	30.107	1.00	49.28
ATOM	1115	CE2	TRP	148	80.966	20.608	31.276	1.00	48.49
ATOM	1116	CE3	TRP	148	78.877	21.222	30.204	1.00	48.27
ATOM	1117	CD1	TRP	148	82.391	20.609	29.557	1.00	48.34
ATOM	1118	NE1	TRP	148	82.269	20.403	30.911	1.00	48.74
ATOM	1119	CZ2	TRP	148	80.358	20.519	32.530	1.00	47.35
ATOM	1120	CZ3	TRP	148	78.271	21.136	31.449	1.00	47.60
ATOM	1121	CH2	TRP	148	79.014	20.787	32.597	1.00	49.76
ATOM	1122	C	TRP	148	79.721	20.293	25.523	1.00	48.75
ATOM	1123	O	TRP	148	78.595	20.765	25.367	1.00	47.54
ATOM	1124	N	LYS	149	80.553	20.059	24.512	1.00	49.96
ATOM	1125	CA	LYS	149	80.179	20.348	23.137	1.00	48.40
ATOM	1126	CB	LYS	149	81.324	19.993	22.203	1.00	52.26
ATOM	1127	CG	LYS	149	82.665	20.533	22.659	1.00	60.02
ATOM	1128	CD	LYS	149	82.621	22.046	22.881	1.00	62.98
ATOM	1129	CE	LYS	149	84.004	22.644	22.710	1.00	64.21
ATOM	1130	NZ	LYS	149	84.536	22.371	21.334	1.00	63.79
ATOM	1131	C	LYS	149	78.947	19.551	22.755	1.00	47.38
ATOM	1132	O	LYS	149	78.135	19.997	21.955	1.00	47.43
ATOM	1133	N	ASP	150	78.801	18.360	23.319	1.00	46.10
ATOM	1134	CA	ASP	150	77.637	17.556	22.994	1.00	45.08
ATOM	1135	CB	ASP	150	77.750	16.163	23.596	1.00	45.12
ATOM	1136	CG	ASP	150	76.718	15.205	23.024	1.00	45.94
ATOM	1137	OD1	ASP	150	76.966	14.701	21.912	1.00	45.25
ATOM	1138	OD2	ASP	150	75.664	14.968	23.664	1.00	42.14
ATOM	1139	C	ASP	150	76.397	18.229	23.565	1.00	45.07
ATOM	1140	O	ASP	150	75.352	18.301	22.916	1.00	45.29
ATOM	1141	N	ILE	151	76.523	18.721	24.791	1.00	43.99
ATOM	1142	CA	ILE	151	75.411	19.371	25.453	1.00	42.56
ATOM	1143	CB	ILE	151	75.757	19.677	26.921	1.00	40.70
ATOM	1144	CG2	ILE	151	74.555	20.304	27.615	1.00	41.16
ATOM	1145	CG1	ILE	151	76.154	18.373	27.635	1.00	40.42
ATOM	1146	CD1	ILE	151	76.586	18.529	29.095	1.00	35.25
ATOM	1147	C	ILE	151	75.018	20.645	24.717	1.00	43.30
ATOM	1148	O	ILE	151	73.838	20.860	24.450	1.00	42.65
ATOM	1149	N	PHE	152	76.003	21.481	24.386	1.00	43.93
ATOM	1150	CA	PHE	152	75.747	22.724	23.658	1.00	44.46
ATOM	1151	CB	PHE	152	77.064	23.426	23.292	1.00	43.79
ATOM	1152	CG	PHE	152	77.805	24.014	24.464	1.00	46.32
ATOM	1153	CD1	PHE	152	79.197	24.083	24.452	1.00	47.49
ATOM	1154	CD2	PHE	152	77.125	24.517	25.570	1.00	47.25
ATOM	1155	CE1	PHE	152	79.903	24.640	25.521	1.00	46.51

ATOM	1156	CE2	PHE	152	77.824	25.079	26.646	1.00	46.64
ATOM	1157	CZ	PHE	152	79.216	25.138	26.618	1.00	46.97
ATOM	1158	C	PHE	152	75.010	22.376	22.370	1.00	44.97
ATOM	1159	O	PHE	152	75.380	21.436	21.672	1.00	45.07
ATOM	1160	N	HIS	153	73.971	23.135	22.054	1.00	47.34
ATOM	1161	CA	HIS	153	73.193	22.913	20.840	1.00	49.91
ATOM	1162	CB	HIS	153	71.905	23.729	20.906	1.00	51.90
ATOM	1163	CG	HIS	153	70.927	23.409	19.821	1.00	52.97
ATOM	1164	CD2	HIS	153	70.035	22.396	19.697	1.00	53.16
ATOM	1165	ND1	HIS	153	70.776	24.194	18.697	1.00	53.71
ATOM	1166	CE1	HIS	153	69.831	23.680	17.931	1.00	55.24
ATOM	1167	NE2	HIS	153	69.365	22.589	18.515	1.00	55.29
ATOM	1168	C	HIS	153	74.004	23.334	19.622	1.00	51.87
ATOM	1169	O	HIS	153	74.923	24.146	19.735	1.00	51.83
ATOM	1170	N	LYS	154	73.673	22.790	18.456	1.00	55.48
ATOM	1171	CA	LYS	154	74.407	23.144	17.247	1.00	60.47
ATOM	1172	CB	LYS	154	73.829	22.445	16.015	1.00	63.01
ATOM	1173	CG	LYS	154	74.206	20.976	15.895	1.00	68.55
ATOM	1174	CD	LYS	154	74.099	20.487	14.449	1.00	73.23
ATOM	1175	CE	LYS	154	72.700	20.712	13.862	1.00	76.00
ATOM	1176	NZ	LYS	154	72.575	20.188	12.467	1.00	75.37
ATOM	1177	C	LYS	154	74.381	24.642	17.024	1.00	62.14
ATOM	1178	O	LYS	154	75.423	25.262	16.808	1.00	63.02
ATOM	1179	N	ASN	155	73.189	25.225	17.095	1.00	63.91
ATOM	1180	CA	ASN	155	73.031	26.659	16.883	1.00	66.44
ATOM	1181	CB	ASN	155	71.566	26.981	16.573	1.00	68.56
ATOM	1182	CG	ASN	155	71.112	26.419	15.230	1.00	71.59
ATOM	1183	OD1	ASN	155	71.122	25.209	15.014	1.00	73.47
ATOM	1184	ND2	ASN	155	70.714	27.304	14.319	1.00	73.15
ATOM	1185	C	ASN	155	73.516	27.532	18.042	1.00	66.84
ATOM	1186	O	ASN	155	73.488	28.762	17.946	1.00	66.67
ATOM	1187	N	ASN	156	73.965	26.912	19.131	1.00	67.57
ATOM	1188	CA	ASN	156	74.440	27.684	20.273	1.00	68.50
ATOM	1189	CB	ASN	156	74.905	26.773	21.412	1.00	66.33
ATOM	1190	CG	ASN	156	75.184	27.542	22.694	1.00	63.56
ATOM	1191	OD1	ASN	156	75.866	28.557	22.678	1.00	62.87
ATOM	1192	ND2	ASN	156	74.662	27.054	23.811	1.00	63.14
ATOM	1193	C	ASN	156	75.595	28.557	19.807	1.00	70.55
ATOM	1194	O	ASN	156	76.671	28.057	19.457	1.00	70.12
ATOM	1195	N	GLN	157	75.350	29.865	19.802	1.00	72.48
ATOM	1196	CA	GLN	157	76.330	30.855	19.369	1.00	73.78
ATOM	1197	CB	GLN	157	75.600	32.098	18.863	1.00	74.49
ATOM	1198	CG	GLN	157	74.721	31.834	17.660	1.00	76.92
ATOM	1199	CD	GLN	157	75.500	31.859	16.363	1.00	79.62
ATOM	1200	OE1	GLN	157	75.897	32.929	15.893	1.00	82.63
ATOM	1201	NE2	GLN	157	75.732	30.683	15.777	1.00	79.15
ATOM	1202	C	GLN	157	77.295	31.251	20.479	1.00	74.47
ATOM	1203	O	GLN	157	78.237	32.013	20.248	1.00	75.49
ATOM	1204	N	LEU	158	77.063	30.728	21.680	1.00	73.60
ATOM	1205	CA	LEU	158	77.904	31.040	22.829	1.00	72.29
ATOM	1206	CB	LEU	158	77.104	31.885	23.820	1.00	71.73
ATOM	1207	CG	LEU	158	76.730	33.257	23.254	1.00	70.67
ATOM	1208	CD1	LEU	158	75.489	33.791	23.939	1.00	71.16
ATOM	1209	CD2	LEU	158	77.910	34.201	23.418	1.00	70.11
ATOM	1210	C	LEU	158	78.444	29.785	23.509	1.00	72.29
ATOM	1211	O	LEU	158	78.572	29.732	24.738	1.00	72.03
ATOM	1212	N	ALA	159	78.761	28.780	22.696	1.00	71.81
ATOM	1213	CA	ALA	159	79.296	27.512	23.188	1.00	70.92
ATOM	1214	CB	ALA	159	79.338	26.489	22.055	1.00	71.11
ATOM	1215	C	ALA	159	80.698	27.749	23.740	1.00	70.01
ATOM	1216	O	ALA	159	81.677	27.176	23.269	1.00	69.90

ATOM	1217	N	LEU	160	80.778	28.609	24.745	1.00	68.85
ATOM	1218	CA	LEU	160	82.040	28.953	25.368	1.00	68.85
ATOM	1219	CB	LEU	160	82.051	30.459	25.652	1.00	69.61
ATOM	1220	CG	LEU	160	83.289	31.167	26.209	1.00	71.41
ATOM	1221	CD1	LEU	160	83.155	32.672	25.979	1.00	70.97
ATOM	1222	CD2	LEU	160	83.448	30.864	27.695	1.00	71.17
ATOM	1223	C	LEU	160	82.201	28.142	26.653	1.00	68.43
ATOM	1224	O	LEU	160	81.221	27.638	27.202	1.00	67.78
ATOM	1225	N	THR	161	83.437	28.007	27.122	1.00	67.93
ATOM	1226	CA	THR	161	83.715	27.252	28.340	1.00	67.32
ATOM	1227	CB	THR	161	84.015	25.769	28.011	1.00	67.61
ATOM	1228	OG1	THR	161	82.822	25.127	27.545	1.00	68.81
ATOM	1229	CG2	THR	161	84.513	25.039	29.236	1.00	69.29
ATOM	1230	C	THR	161	84.883	27.815	29.156	1.00	66.25
ATOM	1231	O	THR	161	85.851	28.342	28.606	1.00	66.57
ATOM	1232	N	LEU	162	84.765	27.709	30.477	1.00	64.73
ATOM	1233	CA	LEU	162	85.797	28.154	31.409	1.00	63.16
ATOM	1234	CB	LEU	162	85.587	29.599	31.844	1.00	63.88
ATOM	1235	CG	LEU	162	86.150	30.685	30.936	1.00	65.76
ATOM	1236	CD1	LEU	162	86.247	31.982	31.736	1.00	64.20
ATOM	1237	CD2	LEU	162	87.533	30.275	30.428	1.00	66.77
ATOM	1238	C	LEU	162	85.699	27.260	32.621	1.00	62.84
ATOM	1239	O	LEU	162	85.062	27.610	33.617	1.00	63.15
ATOM	1240	N	ILE	163	86.339	26.102	32.538	1.00	61.64
ATOM	1241	CA	ILE	163	86.276	25.148	33.622	1.00	61.03
ATOM	1242	CB	ILE	163	85.839	23.779	33.091	1.00	58.91
ATOM	1243	CG2	ILE	163	85.660	22.808	34.245	1.00	57.25
ATOM	1244	CG1	ILE	163	84.527	23.947	32.317	1.00	58.52
ATOM	1245	CD1	ILE	163	84.036	22.705	31.620	1.00	59.29
ATOM	1246	C	ILE	163	87.556	25.004	34.414	1.00	61.98
ATOM	1247	O	ILE	163	88.598	24.637	33.877	1.00	62.41
ATOM	1248	N	ASP	164	87.453	25.303	35.706	1.00	63.32
ATOM	1249	CA	ASP	164	88.567	25.210	36.641	1.00	63.14
ATOM	1250	CB	ASP	164	88.375	26.237	37.768	1.00	61.88
ATOM	1251	CG	ASP	164	89.374	26.069	38.899	1.00	62.81
ATOM	1252	OD1	ASP	164	90.576	25.893	38.605	1.00	62.88
ATOM	1253	OD2	ASP	164	88.961	26.126	40.084	1.00	60.84
ATOM	1254	C	ASP	164	88.584	23.786	37.196	1.00	63.55
ATOM	1255	O	ASP	164	87.533	23.198	37.440	1.00	63.01
ATOM	1256	N	THR	165	89.773	23.224	37.383	1.00	64.53
ATOM	1257	CA	THR	165	89.871	21.868	37.904	1.00	64.48
ATOM	1258	CB	THR	165	90.503	20.924	36.875	1.00	64.86
ATOM	1259	OG1	THR	165	91.734	21.484	36.410	1.00	65.61
ATOM	1260	CG2	THR	165	89.557	20.717	35.695	1.00	64.19
ATOM	1261	C	THR	165	90.638	21.766	39.211	1.00	64.43
ATOM	1262	O	THR	165	90.703	20.691	39.803	1.00	63.97
ATOM	1263	N	ASN	166	91.210	22.878	39.667	1.00	65.17
ATOM	1264	CA	ASN	166	91.945	22.878	40.929	1.00	65.86
ATOM	1265	CB	ASN	166	92.328	24.302	41.359	1.00	68.67
ATOM	1266	CG	ASN	166	93.218	25.006	40.351	1.00	73.52
ATOM	1267	OD1	ASN	166	94.005	24.367	39.651	1.00	71.97
ATOM	1268	ND2	ASN	166	93.109	26.332	40.294	1.00	78.68
ATOM	1269	C	ASN	166	91.058	22.262	42.005	1.00	65.19
ATOM	1270	O	ASN	166	90.106	22.888	42.470	1.00	65.75
ATOM	1271	N	ARG	167	91.368	21.030	42.389	1.00	64.79
ATOM	1272	CA	ARG	167	90.598	20.330	43.408	1.00	64.71
ATOM	1273	CB	ARG	167	90.313	18.897	42.971	1.00	64.49
ATOM	1274	CG	ARG	167	89.594	18.791	41.663	1.00	65.00
ATOM	1275	CD	ARG	167	88.994	17.420	41.511	1.00	65.82
ATOM	1276	NE	ARG	167	88.143	17.344	40.332	1.00	67.22
ATOM	1277	CZ	ARG	167	88.591	17.452	39.089	1.00	68.51

ATOM	1278	NH1	ARG	167	89.883	17.640	38.867	1.00	70.72
ATOM	1279	NH2	ARG	167	87.749	17.365	38.067	1.00	70.00
ATOM	1280	C	ARG	167	91.349	20.299	44.727	1.00	64.78
ATOM	1281	O	ARG	167	92.543	20.583	44.776	1.00	65.42
ATOM	1282	N	SER	168	90.645	19.934	45.792	1.00	64.29
ATOM	1283	CA	SER	168	91.247	19.875	47.112	1.00	63.70
ATOM	1284	CB	SER	168	90.600	20.931	48.010	1.00	64.85
ATOM	1285	OG	SER	168	91.251	21.029	49.262	1.00	63.91
ATOM	1286	C	SER	168	91.078	18.478	47.705	1.00	64.32
ATOM	1287	O	SER	168	91.202	18.281	48.914	1.00	65.24
ATOM	1288	N	ARG	169	90.789	17.511	46.838	1.00	63.72
ATOM	1289	CA	ARG	169	90.618	16.115	47.233	1.00	62.92
ATOM	1290	CB	ARG	169	89.186	15.838	47.700	1.00	61.69
ATOM	1291	CG	ARG	169	88.159	15.928	46.585	1.00	60.81
ATOM	1292	CD	ARG	169	86.850	15.227	46.941	1.00	60.29
ATOM	1293	NE	ARG	169	85.978	15.115	45.771	1.00	60.63
ATOM	1294	CZ	ARG	169	84.979	14.246	45.652	1.00	58.93
ATOM	1295	NH1	ARG	169	84.712	13.403	46.634	1.00	61.04
ATOM	1296	NH2	ARG	169	84.251	14.216	44.544	1.00	58.88
ATOM	1297	C	ARG	169	90.910	15.271	45.999	1.00	63.61
ATOM	1298	O	ARG	169	91.042	15.802	44.896	1.00	64.62
ATOM	1299	N	ALA	170	91.013	13.961	46.182	1.00	63.09
ATOM	1300	CA	ALA	170	91.284	13.061	45.068	1.00	62.15
ATOM	1301	CB	ALA	170	92.188	11.929	45.533	1.00	61.97
ATOM	1302	C	ALA	170	89.964	12.503	44.546	1.00	61.36
ATOM	1303	O	ALA	170	89.064	12.213	45.333	1.00	62.33
ATOM	1304	N	CYS	171	89.843	12.347	43.229	1.00	60.67
ATOM	1305	CA	CYS	171	88.603	11.825	42.650	1.00	60.64
ATOM	1306	C	CYS	171	88.645	10.338	42.335	1.00	60.94
ATOM	1307	O	CYS	171	89.622	9.848	41.773	1.00	60.26
ATOM	1308	CB	CYS	171	88.249	12.547	41.338	1.00	59.51
ATOM	1309	SG	CYS	171	88.141	14.366	41.386	1.00	59.95
ATOM	1310	N	HIS	172	87.589	9.617	42.695	1.00	61.81
ATOM	1311	CA	HIS	172	87.520	8.203	42.347	1.00	62.68
ATOM	1312	CB	HIS	172	86.412	7.488	43.124	1.00	64.14
ATOM	1313	CG	HIS	172	86.736	7.251	44.568	1.00	67.75
ATOM	1314	CD2	HIS	172	87.818	7.591	45.309	1.00	68.32
ATOM	1315	ND1	HIS	172	85.879	6.588	45.422	1.00	68.70
ATOM	1316	CE1	HIS	172	86.418	6.531	46.627	1.00	69.06
ATOM	1317	NE2	HIS	172	87.594	7.132	46.585	1.00	70.47
ATOM	1318	C	HIS	172	87.161	8.243	40.861	1.00	63.27
ATOM	1319	O	HIS	172	86.545	9.200	40.392	1.00	63.84
ATOM	1320	N	PRO	173	87.541	7.213	40.096	1.00	63.36
ATOM	1321	CD	PRO	173	88.332	6.022	40.453	1.00	63.35
ATOM	1322	CA	PRO	173	87.219	7.218	38.666	1.00	62.52
ATOM	1323	CB	PRO	173	88.147	6.139	38.119	1.00	63.08
ATOM	1324	CG	PRO	173	88.152	5.142	39.235	1.00	62.82
ATOM	1325	C	PRO	173	85.745	6.941	38.345	1.00	61.30
ATOM	1326	O	PRO	173	85.018	6.394	39.174	1.00	60.21
ATOM	1327	N	CYS	174	85.319	7.321	37.138	1.00	60.56
ATOM	1328	CA	CYS	174	83.944	7.091	36.694	1.00	60.85
ATOM	1329	C	CYS	174	83.643	5.605	36.800	1.00	62.57
ATOM	1330	O	CYS	174	84.559	4.787	36.806	1.00	64.23
ATOM	1331	CB	CYS	174	83.750	7.506	35.227	1.00	58.70
ATOM	1332	SG	CYS	174	83.709	9.288	34.837	1.00	56.01
ATOM	1333	N	SER	175	82.362	5.254	36.877	1.00	64.18
ATOM	1334	CA	SER	175	81.961	3.852	36.956	1.00	65.15
ATOM	1335	CB	SER	175	80.433	3.738	37.084	1.00	65.03
ATOM	1336	OG	SER	175	79.996	2.385	37.055	1.00	62.93
ATOM	1337	C	SER	175	82.437	3.126	35.689	1.00	66.82
ATOM	1338	O	SER	175	82.599	3.742	34.627	1.00	65.55

ATOM	1339	N	PRO	176	82.677	1.805	35.793	1.00	67.86
ATOM	1340	CD	PRO	176	82.600	0.994	37.021	1.00	67.63
ATOM	1341	CA	PRO	176	83.136	0.991	34.661	1.00	68.04
ATOM	1342	CB	PRO	176	83.251	-0.408	35.266	1.00	68.70
ATOM	1343	CG	PRO	176	83.552	-0.132	36.711	1.00	69.00
ATOM	1344	C	PRO	176	82.126	1.039	33.530	1.00	68.50
ATOM	1345	O	PRO	176	82.476	0.908	32.358	1.00	68.63
ATOM	1346	N	MET	177	80.867	1.233	33.908	1.00	69.98
ATOM	1347	CA	MET	177	79.753	1.307	32.966	1.00	71.03
ATOM	1348	CB	MET	177	78.442	1.427	33.740	1.00	74.07
ATOM	1349	CG	MET	177	78.160	0.279	34.697	1.00	76.88
ATOM	1350	SD	MET	177	77.587	-1.175	33.823	1.00	79.28
ATOM	1351	CE	MET	177	76.129	-0.467	32.980	1.00	76.83
ATOM	1352	C	MET	177	79.860	2.489	32.002	1.00	69.93
ATOM	1353	O	MET	177	79.295	2.452	30.905	1.00	69.07
ATOM	1354	N	CYS	178	80.574	3.535	32.413	1.00	68.38
ATOM	1355	CA	CYS	178	80.721	4.721	31.581	1.00	67.86
ATOM	1356	C	CYS	178	81.723	4.536	30.454	1.00	70.14
ATOM	1357	O	CYS	178	82.929	4.410	30.679	1.00	70.44
ATOM	1358	CB	CYS	178	81.131	5.927	32.419	1.00	64.77
ATOM	1359	SG	CYS	178	79.973	6.377	33.746	1.00	60.59
ATOM	1360	N	LYS	179	81.193	4.552	29.237	1.00	71.44
ATOM	1361	CA	LYS	179	81.961	4.392	28.009	1.00	72.58
ATOM	1362	CB	LYS	179	81.111	4.872	26.823	1.00	74.72
ATOM	1363	CG	LYS	179	79.759	4.447	26.948	1.00	76.95
ATOM	1364	C	LYS	179	83.320	5.107	27.981	1.00	71.24
ATOM	1365	O	LYS	179	84.348	4.529	28.346	1.00	71.78
ATOM	1366	N	GLY	180	83.319	6.362	27.539	1.00	68.84
ATOM	1367	CA	GLY	180	84.557	7.113	27.436	1.00	66.76
ATOM	1368	C	GLY	180	85.009	7.880	28.665	1.00	65.59
ATOM	1369	O	GLY	180	85.504	9.001	28.546	1.00	65.62
ATOM	1370	N	SER	181	84.855	7.284	29.843	1.00	63.98
ATOM	1371	CA	SER	181	85.268	7.942	31.076	1.00	62.30
ATOM	1372	CB	SER	181	86.785	8.155	31.085	1.00	63.70
ATOM	1373	OG	SER	181	87.479	6.920	31.015	1.00	67.09
ATOM	1374	C	SER	181	84.577	9.289	31.233	1.00	60.44
ATOM	1375	O	SER	181	85.179	10.250	31.714	1.00	60.86
ATOM	1376	N	ARG	182	83.316	9.358	30.816	1.00	57.20
ATOM	1377	CA	ARG	182	82.541	10.586	30.922	1.00	53.54
ATOM	1378	CB	ARG	182	81.994	10.977	29.547	1.00	52.60
ATOM	1379	CG	ARG	182	83.079	11.307	28.526	1.00	51.05
ATOM	1380	CD	ARG	182	82.480	11.761	27.208	1.00	49.89
ATOM	1381	NE	ARG	182	83.487	12.061	26.190	1.00	50.63
ATOM	1382	CZ	ARG	182	84.426	12.997	26.313	1.00	53.22
ATOM	1383	NH1	ARG	182	84.501	13.733	27.417	1.00	53.61
ATOM	1384	NH2	ARG	182	85.285	13.213	25.323	1.00	52.35
ATOM	1385	C	ARG	182	81.392	10.399	31.914	1.00	52.13
ATOM	1386	O	ARG	182	80.448	9.652	31.647	1.00	49.98
ATOM	1387	N	CYS	183	81.477	11.067	33.063	1.00	50.35
ATOM	1388	CA	CYS	183	80.424	10.954	34.067	1.00	50.36
ATOM	1389	C	CYS	183	80.235	12.234	34.876	1.00	50.14
ATOM	1390	O	CYS	183	81.110	13.113	34.878	1.00	49.09
ATOM	1391	CB	CYS	183	80.721	9.791	35.017	1.00	51.52
ATOM	1392	SG	CYS	183	82.222	10.011	36.025	1.00	53.52
ATOM	1393	N	TRP	184	79.091	12.326	35.561	1.00	49.39
ATOM	1394	CA	TRP	184	78.754	13.485	36.391	1.00	50.35
ATOM	1395	CB	TRP	184	77.272	13.844	36.280	1.00	48.39
ATOM	1396	CG	TRP	184	76.840	14.320	34.949	1.00	46.10
ATOM	1397	CD2	TRP	184	77.000	15.639	34.425	1.00	46.71
ATOM	1398	CE2	TRP	184	76.450	15.640	33.128	1.00	46.63
ATOM	1399	CE3	TRP	184	77.556	16.825	34.927	1.00	46.81

ATOM	1400	CD1	TRP	184	76.220	13.593	33.981	1.00	44.32
ATOM	1401	NE1	TRP	184	75.982	14.376	32.882	1.00	45.69
ATOM	1402	CZ2	TRP	184	76.436	16.784	32.320	1.00	46.95
ATOM	1403	CZ3	TRP	184	77.545	17.962	34.125	1.00	45.69
ATOM	1404	CH2	TRP	184	76.987	17.932	32.834	1.00	46.50
ATOM	1405	C	TRP	184	79.034	13.182	37.845	1.00	52.63
ATOM	1406	O	TRP	184	78.997	14.072	38.693	1.00	52.34
ATOM	1407	N	GLY	185	79.283	11.912	38.130	1.00	55.68
ATOM	1408	CA	GLY	185	79.559	11.497	39.490	1.00	58.79
ATOM	1409	C	GLY	185	80.110	10.091	39.502	1.00	61.63
ATOM	1410	O	GLY	185	80.183	9.435	38.461	1.00	63.55
ATOM	1411	N	GLU	186	80.498	9.621	40.680	1.00	63.97
ATOM	1412	CA	GLU	186	81.057	8.282	40.821	1.00	65.52
ATOM	1413	CB	GLU	186	81.624	8.113	42.238	1.00	68.21
ATOM	1414	CG	GLU	186	81.996	6.687	42.614	1.00	73.34
ATOM	1415	CD	GLU	186	82.845	6.608	43.877	1.00	76.15
ATOM	1416	OE1	GLU	186	82.521	7.314	44.864	1.00	75.86
ATOM	1417	OE2	GLU	186	83.830	5.829	43.877	1.00	76.23
ATOM	1418	C	GLU	186	80.052	7.172	40.510	1.00	64.74
ATOM	1419	O	GLU	186	80.430	6.108	40.023	1.00	64.79
ATOM	1420	N	SER	187	78.773	7.421	40.768	1.00	64.00
ATOM	1421	CA	SER	187	77.748	6.412	40.524	1.00	64.83
ATOM	1422	CB	SER	187	76.360	6.992	40.784	1.00	64.09
ATOM	1423	OG	SER	187	75.364	6.029	40.506	1.00	65.85
ATOM	1424	C	SER	187	77.781	5.788	39.131	1.00	65.54
ATOM	1425	O	SER	187	78.370	6.334	38.193	1.00	67.53
ATOM	1426	N	SER	188	77.145	4.627	39.011	1.00	65.72
ATOM	1427	CA	SER	188	77.081	3.903	37.747	1.00	65.37
ATOM	1428	CB	SER	188	76.828	2.414	37.997	1.00	65.58
ATOM	1429	OG	SER	188	75.640	2.213	38.745	1.00	66.29
ATOM	1430	C	SER	188	75.941	4.485	36.942	1.00	65.07
ATOM	1431	O	SER	188	75.706	4.102	35.798	1.00	63.32
ATOM	1432	N	GLU	189	75.232	5.419	37.563	1.00	65.54
ATOM	1433	CA	GLU	189	74.108	6.074	36.922	1.00	65.45
ATOM	1434	CB	GLU	189	72.909	6.075	37.863	1.00	68.22
ATOM	1435	CG	GLU	189	72.379	4.704	38.223	1.00	71.35
ATOM	1436	CD	GLU	189	71.195	4.799	39.166	1.00	74.87
ATOM	1437	OE1	GLU	189	70.549	3.760	39.433	1.00	76.57
ATOM	1438	OE2	GLU	189	70.913	5.923	39.645	1.00	74.44
ATOM	1439	C	GLU	189	74.428	7.509	36.522	1.00	63.65
ATOM	1440	O	GLU	189	73.521	8.274	36.198	1.00	64.33
ATOM	1441	N	ASP	190	75.705	7.879	36.543	1.00	61.27
ATOM	1442	CA	ASP	190	76.087	9.237	36.185	1.00	59.70
ATOM	1443	CB	ASP	190	76.898	9.868	37.309	1.00	60.26
ATOM	1444	CG	ASP	190	76.138	9.915	38.607	1.00	62.99
ATOM	1445	OD1	ASP	190	74.995	10.429	38.622	1.00	62.79
ATOM	1446	OD2	ASP	190	76.691	9.440	39.619	1.00	65.30
ATOM	1447	C	ASP	190	76.867	9.339	34.884	1.00	58.34
ATOM	1448	O	ASP	190	77.533	10.344	34.629	1.00	58.18
ATOM	1449	N	CYS	191	76.785	8.305	34.059	1.00	56.49
ATOM	1450	CA	CYS	191	77.491	8.324	32.787	1.00	55.82
ATOM	1451	C	CYS	191	76.855	9.351	31.850	1.00	55.00
ATOM	1452	O	CYS	191	75.640	9.316	31.625	1.00	54.59
ATOM	1453	CB	CYS	191	77.450	6.937	32.142	1.00	56.66
ATOM	1454	SG	CYS	191	78.189	5.611	33.156	1.00	56.79
ATOM	1455	N	GLN	192	77.663	10.269	31.319	1.00	52.00
ATOM	1456	CA	GLN	192	77.144	11.272	30.398	1.00	50.36
ATOM	1457	CB	GLN	192	78.229	12.283	29.975	1.00	48.42
ATOM	1458	CG	GLN	192	77.836	13.130	28.750	1.00	44.65
ATOM	1459	CD	GLN	192	78.811	14.268	28.423	1.00	45.67
ATOM	1460	OE1	GLN	192	79.992	14.214	28.761	1.00	45.08

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ATOM   1461  NE2 GLN   192      78.312  15.294  27.735  1.00 45.93
ATOM   1462  C   GLN   192      76.606  10.573  29.166  1.00 50.85
ATOM   1463  O   GLN   192      77.304   9.789  28.531  1.00 52.31
ATOM   1464  N   SER   193      75.347  10.838  28.848  1.00 50.48
ATOM   1465  CA  SER   193      74.721  10.255  27.674  1.00 50.36
ATOM   1466  CB  SER   193      73.231  10.007  27.941  1.00 51.05
ATOM   1467  OG  SER   193      72.622   9.330  26.856  1.00 54.42
ATOM   1468  C   SER   193      74.896  11.284  26.558  1.00 49.91
ATOM   1469  O   SER   193      74.477  12.437  26.703  1.00 51.97
ATOM   1470  N   LEU   194      75.525  10.885  25.456  1.00 47.52
ATOM   1471  CA  LEU   194      75.743  11.802  24.340  1.00 45.90
ATOM   1472  CB  LEU   194      77.042  11.425  23.618  1.00 45.34
ATOM   1473  CG  LEU   194      78.254  11.307  24.561  1.00 45.76
ATOM   1474  CD1 LEU   194      79.524  10.936  23.792  1.00 46.27
ATOM   1475  CD2 LEU   194      78.453  12.621  25.281  1.00 43.23
ATOM   1476  C   LEU   194      74.541  11.767  23.388  1.00 45.22
ATOM   1477  O   LEU   194      73.954  10.706  23.174  1.00 44.15
ATOM   1478  N   THR   195      74.158  12.922  22.836  1.00 45.06
ATOM   1479  CA  THR   195      73.004  12.977  21.932  1.00 45.39
ATOM   1480  CB  THR   195      71.721  13.462  22.677  1.00 42.78
ATOM   1481  OG1 THR   195      71.877  14.824  23.092  1.00 42.26
ATOM   1482  CG2 THR   195      71.454  12.610  23.888  1.00 40.24
ATOM   1483  C   THR   195      73.188  13.848  20.685  1.00 48.13
ATOM   1484  O   THR   195      72.240  14.046  19.906  1.00 47.32
ATOM   1485  N   ARG   196      74.398  14.366  20.496  1.00 50.47
ATOM   1486  CA  ARG   196      74.700  15.206  19.339  1.00 54.64
ATOM   1487  CB  ARG   196      74.945  16.661  19.774  1.00 55.44
ATOM   1488  CG  ARG   196      75.186  17.639  18.615  1.00 57.51
ATOM   1489  CD  ARG   196      75.521  19.042  19.111  1.00 56.78
ATOM   1490  NE  ARG   196      76.599  19.642  18.328  1.00 60.42
ATOM   1491  CZ  ARG   196      77.246  20.759  18.661  1.00 61.82
ATOM   1492  NH1 ARG   196      76.924  21.413  19.769  1.00 61.40
ATOM   1493  NH2 ARG   196      78.235  21.214  17.897  1.00 61.58
ATOM   1494  C   ARG   196      75.934  14.673  18.611  1.00 56.36
ATOM   1495  O   ARG   196      75.830  14.136  17.514  1.00 56.46
ATOM   1496  N   THR   197      77.097  14.817  19.244  1.00 59.50
ATOM   1497  CA  THR   197      78.374  14.370  18.687  1.00 61.37
ATOM   1498  CB  THR   197      79.531  14.549  19.719  1.00 61.39
ATOM   1499  OG1 THR   197      79.214  13.846  20.927  1.00 63.55
ATOM   1500  CG2 THR   197      79.752  16.020  20.039  1.00 60.20
ATOM   1501  C   THR   197      78.428  12.922  18.167  1.00 62.07
ATOM   1502  O   THR   197      79.360  12.556  17.447  1.00 63.66
ATOM   1503  N   VAL   198      77.450  12.094  18.515  1.00 62.36
ATOM   1504  CA  VAL   198      77.464  10.705  18.051  1.00 63.59
ATOM   1505  CB  VAL   198      77.466   9.733  19.239  1.00 63.41
ATOM   1506  CG1 VAL   198      78.619  10.061  20.169  1.00 65.40
ATOM   1507  CG2 VAL   198      76.141   9.817  19.981  1.00 63.36
ATOM   1508  C   VAL   198      76.269  10.365  17.168  1.00 64.53
ATOM   1509  O   VAL   198      75.768   9.237  17.200  1.00 65.15
ATOM   1510  N   CYS   199      75.820  11.332  16.372  1.00 66.05
ATOM   1511  CA  CYS   199      74.659  11.128  15.511  1.00 67.00
ATOM   1512  C   CYS   199      74.962  10.869  14.040  1.00 69.27
ATOM   1513  O   CYS   199      75.999  11.288  13.510  1.00 67.96
ATOM   1514  CB  CYS   199      73.705  12.325  15.613  1.00 64.26
ATOM   1515  SG  CYS   199      73.095  12.674  17.292  1.00 58.90
ATOM   1516  N   ALA   200      74.024  10.176  13.397  1.00 71.92
ATOM   1517  CA  ALA   200      74.109   9.831  11.984  1.00 74.79
ATOM   1518  CB  ALA   200      73.163   8.670  11.668  1.00 75.33
ATOM   1519  C   ALA   200      73.732  11.052  11.157  1.00 76.31
ATOM   1520  O   ALA   200      73.453  12.119  11.711  1.00 76.44
ATOM   1521  N   GLY   201      73.713  10.887   9.834  1.00 78.51
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ATOM	1522	CA	GLY	201	73.382	11.992	8.952	1.00	78.51
ATOM	1523	C	GLY	201	74.024	13.240	9.517	1.00	79.24
ATOM	1524	O	GLY	201	75.241	13.284	9.716	1.00	79.77
ATOM	1525	N	GLY	202	73.207	14.249	9.801	1.00	78.75
ATOM	1526	CA	GLY	202	73.729	15.475	10.372	1.00	77.26
ATOM	1527	C	GLY	202	72.721	16.040	11.350	1.00	75.70
ATOM	1528	O	GLY	202	72.779	17.222	11.699	1.00	75.31
ATOM	1529	N	CYS	203	71.801	15.192	11.807	1.00	73.40
ATOM	1530	CA	CYS	203	70.758	15.645	12.718	1.00	71.81
ATOM	1531	C	CYS	203	71.308	16.143	14.045	1.00	68.86
ATOM	1532	O	CYS	203	72.292	15.613	14.558	1.00	68.82
ATOM	1533	CB	CYS	203	69.734	14.540	12.948	1.00	72.59
ATOM	1534	SG	CYS	203	70.319	13.145	13.941	1.00	75.84
ATOM	1535	N	ALA	204	70.652	17.169	14.590	1.00	65.90
ATOM	1536	CA	ALA	204	71.050	17.813	15.845	1.00	62.55
ATOM	1537	CB	ALA	204	70.169	19.037	16.091	1.00	60.92
ATOM	1538	C	ALA	204	71.054	16.921	17.087	1.00	60.13
ATOM	1539	O	ALA	204	71.996	16.970	17.880	1.00	60.20
ATOM	1540	N	ARG	205	69.999	16.129	17.261	1.00	57.62
ATOM	1541	CA	ARG	205	69.882	15.233	18.409	1.00	56.05
ATOM	1542	CB	ARG	205	68.831	15.759	19.393	1.00	53.61
ATOM	1543	CG	ARG	205	69.196	17.073	20.070	1.00	52.57
ATOM	1544	CD	ARG	205	70.444	16.932	20.939	1.00	49.89
ATOM	1545	NE	ARG	205	70.879	18.209	21.501	1.00	47.37
ATOM	1546	CZ	ARG	205	72.046	18.391	22.109	1.00	49.35
ATOM	1547	NH1	ARG	205	72.892	17.371	22.236	1.00	51.06
ATOM	1548	NH2	ARG	205	72.378	19.584	22.584	1.00	47.62
ATOM	1549	C	ARG	205	69.499	13.830	17.960	1.00	56.33
ATOM	1550	O	ARG	205	68.872	13.654	16.917	1.00	55.93
ATOM	1551	N	CYS	206	69.866	12.828	18.750	1.00	56.86
ATOM	1552	CA	CYS	206	69.545	11.459	18.383	1.00	59.23
ATOM	1553	C	CYS	206	69.528	10.509	19.578	1.00	62.16
ATOM	1554	O	CYS	206	70.103	10.799	20.625	1.00	62.41
ATOM	1555	CB	CYS	206	70.535	10.970	17.326	1.00	56.45
ATOM	1556	SG	CYS	206	72.269	10.911	17.882	1.00	56.15
ATOM	1557	N	LYS	207	68.848	9.378	19.408	1.00	65.56
ATOM	1558	CA	LYS	207	68.723	8.356	20.445	1.00	68.79
ATOM	1559	CB	LYS	207	67.347	7.683	20.343	1.00	67.04
ATOM	1560	CG	LYS	207	67.173	6.436	21.195	0.01	67.73
ATOM	1561	CD	LYS	207	65.772	5.855	21.043	0.01	67.54
ATOM	1562	CE	LYS	207	65.436	5.561	19.586	0.01	67.59
ATOM	1563	NZ	LYS	207	66.392	4.601	18.974	0.01	67.49
ATOM	1564	C	LYS	207	69.830	7.312	20.293	1.00	71.75
ATOM	1565	O	LYS	207	70.112	6.550	21.218	1.00	72.00
ATOM	1566	N	GLY	208	70.460	7.287	19.123	1.00	74.88
ATOM	1567	CA	GLY	208	71.523	6.330	18.881	1.00	78.08
ATOM	1568	C	GLY	208	72.444	6.705	17.733	1.00	80.40
ATOM	1569	O	GLY	208	72.566	7.880	17.386	1.00	80.35
ATOM	1570	N	PRO	209	73.116	5.718	17.122	1.00	82.07
ATOM	1571	CD	PRO	209	73.269	4.347	17.650	1.00	81.75
ATOM	1572	CA	PRO	209	74.037	5.952	16.004	1.00	82.82
ATOM	1573	CB	PRO	209	75.095	4.884	16.225	1.00	83.11
ATOM	1574	CG	PRO	209	74.248	3.718	16.670	1.00	83.12
ATOM	1575	C	PRO	209	73.388	5.830	14.623	1.00	83.61
ATOM	1576	O	PRO	209	73.866	6.418	13.647	1.00	82.88
ATOM	1577	N	LEU	210	72.302	5.063	14.554	1.00	84.52
ATOM	1578	CA	LEU	210	71.586	4.825	13.301	1.00	86.20
ATOM	1579	CB	LEU	210	70.631	3.640	13.468	1.00	86.91
ATOM	1580	CG	LEU	210	71.320	2.497	13.943	1.00	88.07
ATOM	1581	C	LEU	210	70.799	6.033	12.796	1.00	86.53
ATOM	1582	O	LEU	210	70.273	6.822	13.584	1.00	86.64

ATOM	1583	N	PRO	211	70.705	6.189	11.464	1.00	86.67
ATOM	1584	CD	PRO	211	71.348	5.377	10.417	1.00	86.41
ATOM	1585	CA	PRO	211	69.969	7.313	10.873	1.00	86.21
ATOM	1586	CB	PRO	211	70.054	7.029	9.375	1.00	86.12
ATOM	1587	CG	PRO	211	71.381	6.339	9.249	1.00	86.71
ATOM	1588	C	PRO	211	68.531	7.335	11.378	1.00	84.87
ATOM	1589	O	PRO	211	67.890	8.383	11.416	1.00	84.36
ATOM	1590	N	THR	212	68.038	6.166	11.770	1.00	83.57
ATOM	1591	CA	THR	212	66.680	6.039	12.276	1.00	82.59
ATOM	1592	CB	THR	212	66.202	4.575	12.229	1.00	82.81
ATOM	1593	OG1	THR	212	64.904	4.479	12.833	1.00	83.74
ATOM	1594	CG2	THR	212	67.180	3.671	12.974	1.00	81.77
ATOM	1595	C	THR	212	66.584	6.526	13.713	1.00	81.46
ATOM	1596	O	THR	212	65.499	6.847	14.193	1.00	81.45
ATOM	1597	N	ASP	213	67.720	6.568	14.401	1.00	80.37
ATOM	1598	CA	ASP	213	67.740	7.020	15.788	1.00	79.08
ATOM	1599	CB	ASP	213	69.002	6.524	16.505	1.00	79.78
ATOM	1600	CG	ASP	213	69.053	5.010	16.621	1.00	80.99
ATOM	1601	OD1	ASP	213	68.014	4.400	16.968	1.00	81.86
ATOM	1602	OD2	ASP	213	70.134	4.433	16.374	1.00	80.16
ATOM	1603	C	ASP	213	67.665	8.542	15.874	1.00	77.22
ATOM	1604	O	ASP	213	67.365	9.092	16.935	1.00	77.31
ATOM	1605	N	CYS	214	67.940	9.216	14.759	1.00	74.07
ATOM	1606	CA	CYS	214	67.883	10.672	14.719	1.00	70.05
ATOM	1607	C	CYS	214	66.541	11.159	15.230	1.00	66.41
ATOM	1608	O	CYS	214	65.513	10.513	15.021	1.00	65.64
ATOM	1609	CB	CYS	214	68.084	11.193	13.299	1.00	70.85
ATOM	1610	SG	CYS	214	69.811	11.527	12.823	1.00	76.21
ATOM	1611	N	CYS	215	66.566	12.305	15.902	1.00	62.55
ATOM	1612	CA	CYS	215	65.363	12.913	16.455	1.00	59.05
ATOM	1613	C	CYS	215	64.740	13.900	15.460	1.00	56.72
ATOM	1614	O	CYS	215	65.420	14.435	14.581	1.00	55.51
ATOM	1615	CB	CYS	215	65.697	13.668	17.751	1.00	57.47
ATOM	1616	SG	CYS	215	66.369	12.690	19.136	1.00	53.64
ATOM	1617	N	HIS	216	63.444	14.141	15.607	1.00	54.42
ATOM	1618	CA	HIS	216	62.757	15.096	14.748	1.00	54.48
ATOM	1619	CB	HIS	216	61.269	15.142	15.115	1.00	53.10
ATOM	1620	CG	HIS	216	60.438	15.983	14.195	1.00	55.87
ATOM	1621	CD2	HIS	216	59.589	15.638	13.196	1.00	55.67
ATOM	1622	ND1	HIS	216	60.406	17.360	14.266	1.00	56.51
ATOM	1623	CE1	HIS	216	59.570	17.827	13.354	1.00	56.11
ATOM	1624	NE2	HIS	216	59.061	16.803	12.692	1.00	56.64
ATOM	1625	C	HIS	216	63.410	16.478	14.934	1.00	54.60
ATOM	1626	O	HIS	216	63.856	16.837	16.034	1.00	53.79
ATOM	1627	N	GLU	217	63.470	17.236	13.847	1.00	53.81
ATOM	1628	CA	GLU	217	64.067	18.566	13.833	1.00	54.35
ATOM	1629	CB	GLU	217	63.849	19.193	12.444	1.00	58.36
ATOM	1630	CG	GLU	217	64.190	20.676	12.323	1.00	63.65
ATOM	1631	CD	GLU	217	64.738	21.027	10.948	1.00	67.93
ATOM	1632	OE1	GLU	217	64.097	20.634	9.945	1.00	71.26
ATOM	1633	OE2	GLU	217	65.805	21.692	10.868	1.00	67.02
ATOM	1634	C	GLU	217	63.564	19.513	14.928	1.00	52.90
ATOM	1635	O	GLU	217	64.338	20.313	15.464	1.00	52.25
ATOM	1636	N	GLN	218	62.275	19.421	15.251	1.00	51.31
ATOM	1637	CA	GLN	218	61.661	20.271	16.269	1.00	51.12
ATOM	1638	CB	GLN	218	60.139	20.318	16.080	1.00	50.40
ATOM	1639	CG	GLN	218	59.688	21.323	15.034	1.00	50.78
ATOM	1640	CD	GLN	218	60.338	22.687	15.232	1.00	52.99
ATOM	1641	OE1	GLN	218	60.327	23.238	16.335	1.00	53.76
ATOM	1642	NE2	GLN	218	60.905	23.238	14.164	1.00	52.00
ATOM	1643	C	GLN	218	61.983	19.866	17.705	1.00	51.26

ATOM	1644	O	GLN	218	61.619	20.557	18.654	1.00	51.69
ATOM	1645	N	CYS	219	62.665	18.742	17.863	1.00	51.32
ATOM	1646	CA	CYS	219	63.039	18.271	19.185	1.00	50.59
ATOM	1647	C	CYS	219	64.281	18.988	19.678	1.00	49.99
ATOM	1648	O	CYS	219	65.053	19.540	18.893	1.00	48.92
ATOM	1649	CB	CYS	219	63.369	16.787	19.161	1.00	51.60
ATOM	1650	SG	CYS	219	62.010	15.615	18.926	1.00	53.95
ATOM	1651	N	ALA	220	64.471	18.944	20.991	1.00	49.92
ATOM	1652	CA	ALA	220	65.628	19.530	21.644	1.00	48.74
ATOM	1653	CB	ALA	220	65.293	20.916	22.174	1.00	50.16
ATOM	1654	C	ALA	220	65.995	18.590	22.796	1.00	48.82
ATOM	1655	O	ALA	220	65.121	17.925	23.363	1.00	45.90
ATOM	1656	N	ALA	221	67.286	18.523	23.112	1.00	48.62
ATOM	1657	CA	ALA	221	67.795	17.684	24.195	1.00	49.39
ATOM	1658	CB	ALA	221	67.019	17.963	25.486	1.00	48.33
ATOM	1659	C	ALA	221	67.785	16.183	23.879	1.00	50.36
ATOM	1660	O	ALA	221	68.672	15.444	24.314	1.00	51.30
ATOM	1661	N	GLY	222	66.796	15.720	23.129	1.00	49.99
ATOM	1662	CA	GLY	222	66.770	14.308	22.800	1.00	51.23
ATOM	1663	C	GLY	222	65.397	13.768	22.472	1.00	51.50
ATOM	1664	O	GLY	222	64.432	14.528	22.375	1.00	50.44
ATOM	1665	N	CYS	223	65.306	12.448	22.313	1.00	52.91
ATOM	1666	CA	CYS	223	64.037	11.804	21.979	1.00	54.68
ATOM	1667	C	CYS	223	64.028	10.307	22.259	1.00	55.32
ATOM	1668	O	CYS	223	65.075	9.692	22.470	1.00	55.55
ATOM	1669	CB	CYS	223	63.729	12.016	20.503	1.00	53.19
ATOM	1670	SG	CYS	223	64.960	11.250	19.401	1.00	54.63
ATOM	1671	N	THR	224	62.831	9.729	22.256	1.00	56.47
ATOM	1672	CA	THR	224	62.664	8.296	22.473	1.00	58.28
ATOM	1673	CB	THR	224	61.517	8.008	23.440	1.00	54.80
ATOM	1674	OG1	THR	224	60.305	8.560	22.917	1.00	50.55
ATOM	1675	CG2	THR	224	61.812	8.620	24.796	1.00	53.35
ATOM	1676	C	THR	224	62.335	7.677	21.117	1.00	61.82
ATOM	1677	O	THR	224	62.844	6.613	20.758	1.00	63.89
ATOM	1678	N	GLY	225	61.480	8.364	20.367	1.00	64.77
ATOM	1679	CA	GLY	225	61.100	7.899	19.044	1.00	66.41
ATOM	1680	C	GLY	225	61.548	8.883	17.973	1.00	66.85
ATOM	1681	O	GLY	225	62.223	9.873	18.275	1.00	66.37
ATOM	1682	N	PRO	226	61.195	8.633	16.705	1.00	66.86
ATOM	1683	CD	PRO	226	60.659	7.353	16.199	1.00	66.51
ATOM	1684	CA	PRO	226	61.575	9.521	15.599	1.00	66.01
ATOM	1685	CB	PRO	226	61.713	8.556	14.431	1.00	67.21
ATOM	1686	CG	PRO	226	60.571	7.596	14.694	1.00	67.17
ATOM	1687	C	PRO	226	60.537	10.615	15.319	1.00	64.69
ATOM	1688	O	PRO	226	60.805	11.560	14.577	1.00	63.09
ATOM	1689	N	LYS	227	59.356	10.478	15.917	1.00	63.65
ATOM	1690	CA	LYS	227	58.276	11.438	15.716	1.00	63.98
ATOM	1691	CB	LYS	227	56.930	10.785	16.082	1.00	64.77
ATOM	1692	CG	LYS	227	56.580	9.579	15.200	1.00	66.25
ATOM	1693	CD	LYS	227	55.152	9.061	15.416	1.00	69.05
ATOM	1694	CE	LYS	227	54.965	8.378	16.775	1.00	70.66
ATOM	1695	NZ	LYS	227	55.844	7.181	16.951	1.00	70.84
ATOM	1696	C	LYS	227	58.467	12.748	16.487	1.00	63.25
ATOM	1697	O	LYS	227	59.191	12.792	17.485	1.00	62.89
ATOM	1698	N	HIS	228	57.823	13.815	16.014	1.00	61.92
ATOM	1699	CA	HIS	228	57.927	15.117	16.665	1.00	61.52
ATOM	1700	CB	HIS	228	57.443	16.236	15.721	1.00	61.00
ATOM	1701	CG	HIS	228	55.996	16.149	15.342	1.00	62.26
ATOM	1702	CD2	HIS	228	55.015	15.296	15.728	1.00	62.88
ATOM	1703	ND1	HIS	228	55.404	17.043	14.477	1.00	62.93
ATOM	1704	CE1	HIS	228	54.123	16.748	14.347	1.00	62.35

ATOM	1705	NE2	HIS	228	53.861	15.692	15.097	1.00	62.26
ATOM	1706	C	HIS	228	57.133	15.114	17.972	1.00	61.48
ATOM	1707	O	HIS	228	56.898	16.156	18.589	1.00	60.05
ATOM	1708	N	SER	229	56.733	13.915	18.384	1.00	61.60
ATOM	1709	CA	SER	229	55.969	13.713	19.609	1.00	61.01
ATOM	1710	CB	SER	229	54.644	13.010	19.286	1.00	61.25
ATOM	1711	OG	SER	229	54.855	11.816	18.539	1.00	61.44
ATOM	1712	C	SER	229	56.783	12.871	20.591	1.00	59.99
ATOM	1713	O	SER	229	56.332	12.581	21.698	1.00	59.55
ATOM	1714	N	ASP	230	57.984	12.482	20.174	1.00	59.28
ATOM	1715	CA	ASP	230	58.866	11.674	21.011	1.00	59.27
ATOM	1716	CB	ASP	230	59.423	10.492	20.212	1.00	60.87
ATOM	1717	CG	ASP	230	58.346	9.719	19.479	1.00	62.55
ATOM	1718	OD1	ASP	230	57.331	9.352	20.118	1.00	62.34
ATOM	1719	OD2	ASP	230	58.525	9.473	18.263	1.00	62.79
ATOM	1720	C	ASP	230	60.031	12.511	21.535	1.00	58.31
ATOM	1721	O	ASP	230	61.065	11.980	21.945	1.00	59.10
ATOM	1722	N	CYS	231	59.863	13.826	21.501	1.00	56.84
ATOM	1723	CA	CYS	231	60.889	14.741	21.969	1.00	53.72
ATOM	1724	C	CYS	231	60.990	14.742	23.497	1.00	52.21
ATOM	1725	O	CYS	231	59.996	14.525	24.200	1.00	49.54
ATOM	1726	CB	CYS	231	60.562	16.166	21.524	1.00	54.60
ATOM	1727	SG	CYS	231	60.392	16.502	19.744	1.00	53.23
ATOM	1728	N	LEU	232	62.191	14.992	24.009	1.00	50.70
ATOM	1729	CA	LEU	232	62.382	15.078	25.452	1.00	50.35
ATOM	1730	CB	LEU	232	63.822	14.746	25.836	1.00	49.26
ATOM	1731	CG	LEU	232	64.221	13.274	25.726	1.00	51.66
ATOM	1732	CD1	LEU	232	65.665	13.105	26.204	1.00	50.91
ATOM	1733	CD2	LEU	232	63.279	12.416	26.561	1.00	49.83
ATOM	1734	C	LEU	232	62.064	16.514	25.856	1.00	49.63
ATOM	1735	O	LEU	232	61.730	16.798	27.003	1.00	49.78
ATOM	1736	N	ALA	233	62.178	17.414	24.887	1.00	50.22
ATOM	1737	CA	ALA	233	61.910	18.834	25.084	1.00	49.90
ATOM	1738	CB	ALA	233	63.099	19.507	25.759	1.00	49.52
ATOM	1739	C	ALA	233	61.692	19.441	23.711	1.00	49.74
ATOM	1740	O	ALA	233	62.251	18.962	22.718	1.00	50.22
ATOM	1741	N	CYS	234	60.883	20.493	23.654	1.00	48.80
ATOM	1742	CA	CYS	234	60.605	21.168	22.391	1.00	46.07
ATOM	1743	C	CYS	234	61.573	22.320	22.159	1.00	45.21
ATOM	1744	O	CYS	234	61.745	23.189	23.019	1.00	44.39
ATOM	1745	CB	CYS	234	59.182	21.704	22.383	1.00	44.96
ATOM	1746	SG	CYS	234	57.878	20.445	22.262	1.00	49.23
ATOM	1747	N	LEU	235	62.206	22.321	20.991	1.00	44.46
ATOM	1748	CA	LEU	235	63.154	23.373	20.635	1.00	42.64
ATOM	1749	CB	LEU	235	63.753	23.087	19.259	1.00	38.15
ATOM	1750	CG	LEU	235	64.722	24.119	18.670	1.00	40.61
ATOM	1751	CD1	LEU	235	65.957	24.301	19.542	1.00	38.57
ATOM	1752	CD2	LEU	235	65.127	23.644	17.284	1.00	39.44
ATOM	1753	C	LEU	235	62.486	24.753	20.647	1.00	42.98
ATOM	1754	O	LEU	235	63.126	25.748	20.976	1.00	44.50
ATOM	1755	N	HIS	236	61.200	24.805	20.300	1.00	43.28
ATOM	1756	CA	HIS	236	60.448	26.064	20.273	1.00	43.13
ATOM	1757	CB	HIS	236	60.140	26.472	18.828	1.00	41.66
ATOM	1758	CG	HIS	236	61.362	26.675	17.981	1.00	41.09
ATOM	1759	CD2	HIS	236	61.972	25.857	17.093	1.00	37.73
ATOM	1760	ND1	HIS	236	62.124	27.825	18.032	1.00	39.96
ATOM	1761	CE1	HIS	236	63.151	27.704	17.212	1.00	38.38
ATOM	1762	NE2	HIS	236	63.082	26.519	16.631	1.00	38.79
ATOM	1763	C	HIS	236	59.136	25.958	21.048	1.00	43.69
ATOM	1764	O	HIS	236	59.016	26.492	22.140	1.00	43.60
ATOM	1765	N	PHE	237	58.148	25.259	20.501	1.00	45.04

ATOM	1766	CA	PHE	237	56.881	25.168	21.208	1.00	47.08
ATOM	1767	CB	PHE	237	55.866	26.126	20.576	1.00	46.02
ATOM	1768	CG	PHE	237	56.309	27.549	20.593	1.00	44.88
ATOM	1769	CD1	PHE	237	56.765	28.160	19.435	1.00	44.85
ATOM	1770	CD2	PHE	237	56.337	28.262	21.786	1.00	43.81
ATOM	1771	CE1	PHE	237	57.248	29.467	19.465	1.00	45.44
ATOM	1772	CE2	PHE	237	56.820	29.569	21.830	1.00	43.85
ATOM	1773	CZ	PHE	237	57.276	30.174	20.670	1.00	44.65
ATOM	1774	C	PHE	237	56.244	23.804	21.335	1.00	48.24
ATOM	1775	O	PHE	237	56.268	23.002	20.405	1.00	50.43
ATOM	1776	N	ASN	238	55.681	23.543	22.508	1.00	49.47
ATOM	1777	CA	ASN	238	54.973	22.296	22.741	1.00	51.45
ATOM	1778	CB	ASN	238	55.082	21.856	24.202	1.00	54.33
ATOM	1779	CG	ASN	238	54.388	20.529	24.458	1.00	59.95
ATOM	1780	OD1	ASN	238	53.556	20.093	23.652	1.00	61.47
ATOM	1781	ND2	ASN	238	54.713	19.885	25.579	1.00	63.18
ATOM	1782	C	ASN	238	53.526	22.658	22.418	1.00	50.77
ATOM	1783	O	ASN	238	52.926	23.500	23.089	1.00	49.69
ATOM	1784	N	HIS	239	52.983	22.049	21.372	1.00	50.70
ATOM	1785	CA	HIS	239	51.616	22.319	20.953	1.00	51.93
ATOM	1786	CB	HIS	239	51.581	22.562	19.443	1.00	51.88
ATOM	1787	CG	HIS	239	50.227	22.916	18.912	1.00	52.05
ATOM	1788	CD2	HIS	239	49.115	23.373	19.533	1.00	50.98
ATOM	1789	ND1	HIS	239	49.913	22.838	17.571	1.00	53.11
ATOM	1790	CE1	HIS	239	48.664	23.234	17.392	1.00	52.58
ATOM	1791	NE2	HIS	239	48.159	23.564	18.566	1.00	50.88
ATOM	1792	C	HIS	239	50.728	21.134	21.313	1.00	54.08
ATOM	1793	O	HIS	239	50.366	20.324	20.455	1.00	55.11
ATOM	1794	N	SER	240	50.390	21.025	22.590	1.00	55.26
ATOM	1795	CA	SER	240	49.547	19.932	23.046	1.00	57.11
ATOM	1796	CB	SER	240	48.118	20.101	22.510	1.00	57.75
ATOM	1797	OG	SER	240	47.417	21.127	23.197	1.00	60.07
ATOM	1798	C	SER	240	50.086	18.567	22.619	1.00	57.00
ATOM	1799	O	SER	240	49.352	17.756	22.058	1.00	57.19
ATOM	1800	N	GLY	241	51.366	18.314	22.870	1.00	56.21
ATOM	1801	CA	GLY	241	51.921	17.022	22.514	1.00	55.65
ATOM	1802	C	GLY	241	52.931	17.001	21.384	1.00	56.21
ATOM	1803	O	GLY	241	53.783	16.108	21.332	1.00	56.34
ATOM	1804	N	ILE	242	52.850	17.959	20.467	1.00	55.70
ATOM	1805	CA	ILE	242	53.804	17.982	19.368	1.00	56.07
ATOM	1806	CB	ILE	242	53.100	17.806	17.992	1.00	57.14
ATOM	1807	CG2	ILE	242	52.197	16.579	18.027	1.00	58.47
ATOM	1808	CG1	ILE	242	52.266	19.035	17.653	1.00	57.33
ATOM	1809	CD1	ILE	242	51.636	18.967	16.284	1.00	59.21
ATOM	1810	C	ILE	242	54.632	19.264	19.355	1.00	54.41
ATOM	1811	O	ILE	242	54.119	20.352	19.594	1.00	54.64
ATOM	1812	N	CYS	243	55.925	19.118	19.098	1.00	52.85
ATOM	1813	CA	CYS	243	56.824	20.258	19.045	1.00	51.87
ATOM	1814	C	CYS	243	56.746	20.886	17.658	1.00	52.41
ATOM	1815	O	CYS	243	56.821	20.184	16.649	1.00	52.32
ATOM	1816	CB	CYS	243	58.268	19.818	19.310	1.00	51.08
ATOM	1817	SG	CYS	243	58.637	19.090	20.946	1.00	46.96
ATOM	1818	N	GLU	244	56.598	22.207	17.612	1.00	52.51
ATOM	1819	CA	GLU	244	56.521	22.935	16.349	1.00	52.16
ATOM	1820	CB	GLU	244	55.057	23.264	16.028	1.00	55.07
ATOM	1821	CG	GLU	244	54.287	22.078	15.419	1.00	57.94
ATOM	1822	CD	GLU	244	52.773	22.235	15.473	1.00	59.16
ATOM	1823	OE1	GLU	244	52.070	21.444	14.813	1.00	61.89
ATOM	1824	OE2	GLU	244	52.280	23.133	16.180	1.00	60.11
ATOM	1825	C	GLU	244	57.362	24.210	16.398	1.00	50.67
ATOM	1826	O	GLU	244	57.778	24.650	17.477	1.00	50.55

ATOM	1827	N	LEU	245	57.626	24.792	15.229	1.00	47.79
ATOM	1828	CA	LEU	245	58.418	26.019	15.143	1.00	45.05
ATOM	1829	CB	LEU	245	58.850	26.268	13.697	1.00	44.16
ATOM	1830	CG	LEU	245	59.673	27.522	13.385	1.00	46.91
ATOM	1831	CD1	LEU	245	61.006	27.525	14.158	1.00	46.09
ATOM	1832	CD2	LEU	245	59.921	27.569	11.887	1.00	44.84
ATOM	1833	C	LEU	245	57.641	27.226	15.684	1.00	43.01
ATOM	1834	O	LEU	245	58.227	28.138	16.254	1.00	43.29
ATOM	1835	N	HIS	246	56.328	27.245	15.498	1.00	42.54
ATOM	1836	CA	HIS	246	55.516	28.336	16.033	1.00	43.79
ATOM	1837	CB	HIS	246	55.446	29.533	15.066	1.00	43.90
ATOM	1838	CG	HIS	246	54.822	29.218	13.744	1.00	46.48
ATOM	1839	CD2	HIS	246	55.345	29.205	12.493	1.00	47.31
ATOM	1840	ND1	HIS	246	53.504	28.832	13.613	1.00	46.81
ATOM	1841	CE1	HIS	246	53.244	28.591	12.339	1.00	48.43
ATOM	1842	NE2	HIS	246	54.343	28.809	11.639	1.00	47.81
ATOM	1843	C	HIS	246	54.122	27.822	16.345	1.00	43.37
ATOM	1844	O	HIS	246	53.756	26.727	15.936	1.00	42.87
ATOM	1845	N	CYS	247	53.352	28.607	17.086	1.00	44.91
ATOM	1846	CA	CYS	247	52.001	28.198	17.441	1.00	46.69
ATOM	1847	C	CYS	247	51.029	28.620	16.363	1.00	46.85
ATOM	1848	O	CYS	247	51.390	29.345	15.440	1.00	47.26
ATOM	1849	CB	CYS	247	51.574	28.828	18.766	1.00	45.32
ATOM	1850	SG	CYS	247	52.606	28.367	20.196	1.00	48.87
ATOM	1851	N	PRO	248	49.777	28.155	16.458	1.00	47.67
ATOM	1852	CD	PRO	248	49.277	27.029	17.261	1.00	48.14
ATOM	1853	CA	PRO	248	48.792	28.539	15.447	1.00	48.14
ATOM	1854	CB	PRO	248	47.665	27.525	15.650	1.00	47.79
ATOM	1855	CG	PRO	248	48.355	26.353	16.284	1.00	48.90
ATOM	1856	C	PRO	248	48.339	29.954	15.770	1.00	48.84
ATOM	1857	O	PRO	248	47.903	30.219	16.888	1.00	49.62
ATOM	1858	N	ALA	249	48.448	30.857	14.806	1.00	49.08
ATOM	1859	CA	ALA	249	48.029	32.239	15.012	1.00	51.41
ATOM	1860	CB	ALA	249	48.198	33.025	13.711	1.00	51.96
ATOM	1861	C	ALA	249	46.576	32.337	15.507	1.00	51.87
ATOM	1862	O	ALA	249	45.776	31.417	15.326	1.00	51.47
ATOM	1863	N	LEU	250	46.245	33.458	16.139	1.00	53.36
ATOM	1864	CA	LEU	250	44.898	33.677	16.656	1.00	55.64
ATOM	1865	CB	LEU	250	44.905	34.778	17.720	1.00	54.87
ATOM	1866	CG	LEU	250	45.630	34.462	19.021	1.00	54.91
ATOM	1867	CD1	LEU	250	45.485	35.628	19.978	1.00	56.42
ATOM	1868	CD2	LEU	250	45.049	33.202	19.631	1.00	56.57
ATOM	1869	C	LEU	250	43.902	34.060	15.566	1.00	56.65
ATOM	1870	O	LEU	250	42.691	33.966	15.760	1.00	55.99
ATOM	1871	N	VAL	251	44.405	34.499	14.422	1.00	58.57
ATOM	1872	CA	VAL	251	43.512	34.896	13.347	1.00	61.37
ATOM	1873	CB	VAL	251	43.509	36.425	13.164	1.00	61.36
ATOM	1874	CG1	VAL	251	43.124	37.110	14.470	1.00	59.22
ATOM	1875	CG2	VAL	251	44.883	36.889	12.694	1.00	61.93
ATOM	1876	C	VAL	251	43.886	34.276	12.018	1.00	63.15
ATOM	1877	O	VAL	251	45.061	34.033	11.746	1.00	64.19
ATOM	1878	N	THR	252	42.873	34.013	11.199	1.00	65.01
ATOM	1879	CA	THR	252	43.076	33.461	9.865	1.00	66.08
ATOM	1880	CB	THR	252	42.151	32.259	9.584	1.00	67.82
ATOM	1881	OG1	THR	252	42.265	31.301	10.640	1.00	70.86
ATOM	1882	CG2	THR	252	42.532	31.590	8.272	1.00	68.46
ATOM	1883	C	THR	252	42.660	34.601	8.946	1.00	65.57
ATOM	1884	O	THR	252	41.695	35.311	9.248	1.00	66.04
ATOM	1885	N	TYR	253	43.379	34.796	7.845	1.00	63.88
ATOM	1886	CA	TYR	253	43.024	35.864	6.922	1.00	62.24
ATOM	1887	CB	TYR	253	44.272	36.620	6.463	1.00	61.85

ATOM	1888	CG	TYR	253	44.977	37.329	7.592	1.00	62.35
ATOM	1889	CD1	TYR	253	46.223	36.891	8.046	1.00	61.84
ATOM	1890	CE1	TYR	253	46.859	37.517	9.113	1.00	61.95
ATOM	1891	CD2	TYR	253	44.382	38.416	8.237	1.00	61.08
ATOM	1892	CE2	TYR	253	45.007	39.048	9.307	1.00	61.11
ATOM	1893	CZ	TYR	253	46.245	38.594	9.740	1.00	62.39
ATOM	1894	OH	TYR	253	46.873	39.213	10.797	1.00	63.23
ATOM	1895	C	TYR	253	42.250	35.362	5.713	1.00	60.86
ATOM	1896	O	TYR	253	42.409	34.215	5.283	1.00	58.01
ATOM	1897	N	ASN	254	41.403	36.242	5.183	1.00	60.70
ATOM	1898	CA	ASN	254	40.587	35.942	4.020	1.00	61.15
ATOM	1899	CB	ASN	254	39.425	36.939	3.922	1.00	62.18
ATOM	1900	CG	ASN	254	38.575	36.728	2.675	1.00	63.32
ATOM	1901	OD1	ASN	254	38.771	37.386	1.648	1.00	60.67
ATOM	1902	ND2	ASN	254	37.636	35.792	2.757	1.00	63.52
ATOM	1903	C	ASN	254	41.450	36.013	2.764	1.00	61.98
ATOM	1904	O	ASN	254	42.152	37.002	2.529	1.00	60.65
ATOM	1905	N	THR	255	41.385	34.954	1.965	1.00	62.41
ATOM	1906	CA	THR	255	42.149	34.841	0.726	1.00	63.35
ATOM	1907	CB	THR	255	41.705	33.572	-0.030	1.00	63.45
ATOM	1908	OG1	THR	255	42.419	32.447	0.496	1.00	63.38
ATOM	1909	CG2	THR	255	41.947	33.700	-1.535	1.00	63.89
ATOM	1910	C	THR	255	42.098	36.045	-0.220	1.00	64.24
ATOM	1911	O	THR	255	43.107	36.404	-0.826	1.00	63.50
ATOM	1912	N	ASP	256	40.929	36.669	-0.337	1.00	66.28
ATOM	1913	CA	ASP	256	40.753	37.806	-1.239	1.00	68.16
ATOM	1914	CB	ASP	256	39.442	37.660	-2.018	1.00	69.86
ATOM	1915	CG	ASP	256	39.327	36.325	-2.722	1.00	72.07
ATOM	1916	OD1	ASP	256	40.068	36.111	-3.712	1.00	73.36
ATOM	1917	OD2	ASP	256	38.501	35.490	-2.277	1.00	71.56
ATOM	1918	C	ASP	256	40.725	39.139	-0.527	1.00	69.08
ATOM	1919	O	ASP	256	41.317	40.115	-0.984	1.00	69.16
ATOM	1920	N	THR	257	40.020	39.176	0.593	1.00	70.47
ATOM	1921	CA	THR	257	39.874	40.400	1.357	1.00	72.75
ATOM	1922	CB	THR	257	38.563	40.381	2.149	1.00	73.56
ATOM	1923	OG1	THR	257	37.564	39.674	1.403	1.00	74.14
ATOM	1924	CG2	THR	257	38.086	41.791	2.403	1.00	73.14
ATOM	1925	C	THR	257	41.004	40.626	2.344	1.00	73.48
ATOM	1926	O	THR	257	41.428	41.760	2.568	1.00	74.03
ATOM	1927	N	PHE	258	41.492	39.537	2.927	1.00	74.08
ATOM	1928	CA	PHE	258	42.540	39.608	3.933	1.00	74.96
ATOM	1929	CB	PHE	258	43.801	40.300	3.396	1.00	73.47
ATOM	1930	CG	PHE	258	44.676	39.383	2.594	1.00	73.25
ATOM	1931	CD1	PHE	258	44.419	39.154	1.248	1.00	72.60
ATOM	1932	CD2	PHE	258	45.701	38.670	3.208	1.00	72.78
ATOM	1933	CE1	PHE	258	45.163	38.223	0.526	1.00	73.28
ATOM	1934	CE2	PHE	258	46.450	37.738	2.496	1.00	71.82
ATOM	1935	CZ	PHE	258	46.179	37.511	1.153	1.00	72.81
ATOM	1936	C	PHE	258	41.991	40.339	5.140	1.00	76.08
ATOM	1937	O	PHE	258	42.578	41.298	5.639	1.00	75.95
ATOM	1938	N	GLU	259	40.829	39.878	5.579	1.00	78.07
ATOM	1939	CA	GLU	259	40.171	40.435	6.740	1.00	80.33
ATOM	1940	CB	GLU	259	38.744	40.869	6.403	1.00	82.99
ATOM	1941	CG	GLU	259	38.635	42.348	6.032	1.00	88.00
ATOM	1942	CD	GLU	259	37.196	42.806	5.809	1.00	90.89
ATOM	1943	OE1	GLU	259	36.577	42.381	4.807	1.00	91.78
ATOM	1944	OE2	GLU	259	36.684	43.590	6.641	1.00	92.51
ATOM	1945	C	GLU	259	40.166	39.351	7.802	1.00	80.14
ATOM	1946	O	GLU	259	39.849	38.192	7.519	1.00	80.17
ATOM	1947	N	SER	260	40.535	39.741	9.018	1.00	79.91
ATOM	1948	CA	SER	260	40.613	38.830	10.152	1.00	79.51

ATOM	1949	CB	SER	260	40.948	39.603	11.435	1.00	79.83
ATOM	1950	OG	SER	260	42.295	40.041	11.451	1.00	82.07
ATOM	1951	C	SER	260	39.383	37.982	10.417	1.00	79.07
ATOM	1952	O	SER	260	38.247	38.383	10.162	1.00	78.31
ATOM	1953	N	MET	261	39.647	36.795	10.947	1.00	79.30
ATOM	1954	CA	MET	261	38.629	35.836	11.332	1.00	79.39
ATOM	1955	CB	MET	261	38.224	34.946	10.149	1.00	82.44
ATOM	1956	CG	MET	261	37.133	35.551	9.255	1.00	86.60
ATOM	1957	SD	MET	261	35.583	35.989	10.146	1.00	89.52
ATOM	1958	CE	MET	261	34.711	34.386	10.152	1.00	88.94
ATOM	1959	C	MET	261	39.249	35.004	12.446	1.00	77.40
ATOM	1960	O	MET	261	40.337	34.443	12.285	1.00	76.93
ATOM	1961	N	PRO	262	38.574	34.931	13.601	1.00	75.08
ATOM	1962	CD	PRO	262	37.184	35.340	13.847	1.00	74.38
ATOM	1963	CA	PRO	262	39.089	34.158	14.732	1.00	73.19
ATOM	1964	CB	PRO	262	37.940	34.212	15.734	1.00	73.46
ATOM	1965	CG	PRO	262	36.740	34.314	14.858	1.00	74.32
ATOM	1966	C	PRO	262	39.463	32.737	14.333	1.00	71.04
ATOM	1967	O	PRO	262	38.839	32.140	13.454	1.00	70.71
ATOM	1968	N	ASN	263	40.496	32.210	14.978	1.00	68.58
ATOM	1969	CA	ASN	263	40.962	30.864	14.689	1.00	67.27
ATOM	1970	CB	ASN	263	42.470	30.865	14.436	1.00	66.62
ATOM	1971	CG	ASN	263	42.986	29.507	14.004	1.00	65.52
ATOM	1972	OD1	ASN	263	42.506	28.474	14.462	1.00	65.69
ATOM	1973	ND2	ASN	263	43.980	29.502	13.129	1.00	65.08
ATOM	1974	C	ASN	263	40.653	29.941	15.857	1.00	66.33
ATOM	1975	O	ASN	263	41.212	30.099	16.941	1.00	65.65
ATOM	1976	N	PRO	264	39.761	28.959	15.647	1.00	66.51
ATOM	1977	CD	PRO	264	39.157	28.575	14.357	1.00	65.55
ATOM	1978	CA	PRO	264	39.390	28.010	16.702	1.00	65.99
ATOM	1979	CB	PRO	264	38.407	27.078	15.991	1.00	66.25
ATOM	1980	CG	PRO	264	38.883	27.105	14.561	1.00	65.20
ATOM	1981	C	PRO	264	40.612	27.267	17.251	1.00	66.56
ATOM	1982	O	PRO	264	40.627	26.838	18.407	1.00	65.94
ATOM	1983	N	GLU	265	41.637	27.131	16.411	1.00	66.53
ATOM	1984	CA	GLU	265	42.872	26.450	16.781	1.00	65.73
ATOM	1985	CB	GLU	265	43.401	25.655	15.585	1.00	68.14
ATOM	1986	CG	GLU	265	42.471	24.553	15.090	1.00	72.53
ATOM	1987	CD	GLU	265	42.368	23.379	16.059	1.00	76.42
ATOM	1988	OE1	GLU	265	43.414	22.773	16.391	1.00	78.03
ATOM	1989	OE2	GLU	265	41.238	23.057	16.487	1.00	78.72
ATOM	1990	C	GLU	265	43.940	27.440	17.250	1.00	63.96
ATOM	1991	O	GLU	265	45.083	27.057	17.509	1.00	63.86
ATOM	1992	N	GLY	266	43.566	28.710	17.356	1.00	61.36
ATOM	1993	CA	GLY	266	44.514	29.722	17.789	1.00	58.94
ATOM	1994	C	GLY	266	44.947	29.550	19.231	1.00	57.21
ATOM	1995	O	GLY	266	44.139	29.165	20.071	1.00	57.33
ATOM	1996	N	ARG	267	46.222	29.830	19.511	1.00	56.18
ATOM	1997	CA	ARG	267	46.793	29.724	20.861	1.00	53.52
ATOM	1998	CB	ARG	267	47.494	28.376	21.049	1.00	55.28
ATOM	1999	CG	ARG	267	46.634	27.156	20.756	1.00	59.39
ATOM	2000	CD	ARG	267	45.362	27.124	21.604	1.00	61.46
ATOM	2001	NE	ARG	267	44.597	25.914	21.346	1.00	61.95
ATOM	2002	CZ	ARG	267	45.085	24.696	21.543	1.00	66.21
ATOM	2003	NH1	ARG	267	46.326	24.547	21.999	1.00	66.55
ATOM	2004	NH2	ARG	267	44.347	23.626	21.280	1.00	66.39
ATOM	2005	C	ARG	267	47.827	30.824	21.096	1.00	52.01
ATOM	2006	O	ARG	267	48.474	31.287	20.153	1.00	50.48
ATOM	2007	N	TYR	268	47.988	31.247	22.347	1.00	49.34
ATOM	2008	CA	TYR	268	48.990	32.267	22.645	1.00	48.57
ATOM	2009	CB	TYR	268	48.583	33.135	23.838	1.00	49.99

ATOM	2010	CG	TYR	268	47.271	33.870	23.686	1.00	50.84
ATOM	2011	CD1	TYR	268	46.055	33.181	23.695	1.00	50.27
ATOM	2012	CE1	TYR	268	44.847	33.853	23.549	1.00	50.81
ATOM	2013	CD2	TYR	268	47.245	35.253	23.533	1.00	49.75
ATOM	2014	CE2	TYR	268	46.044	35.937	23.387	1.00	51.75
ATOM	2015	CZ	TYR	268	44.849	35.231	23.393	1.00	52.26
ATOM	2016	OH	TYR	268	43.661	35.903	23.213	1.00	54.20
ATOM	2017	C	TYR	268	50.324	31.594	22.975	1.00	48.52
ATOM	2018	O	TYR	268	50.384	30.390	23.261	1.00	46.36
ATOM	2019	N	THR	269	51.397	32.376	22.920	1.00	48.17
ATOM	2020	CA	THR	269	52.707	31.853	23.252	1.00	46.34
ATOM	2021	CB	THR	269	53.817	32.473	22.379	1.00	44.79
ATOM	2022	OG1	THR	269	53.783	33.898	22.488	1.00	45.68
ATOM	2023	CG2	THR	269	53.632	32.083	20.938	1.00	45.34
ATOM	2024	C	THR	269	52.960	32.186	24.721	1.00	47.04
ATOM	2025	O	THR	269	52.713	33.309	25.170	1.00	47.56
ATOM	2026	N	PHE	270	53.411	31.186	25.469	1.00	45.80
ATOM	2027	CA	PHE	270	53.719	31.342	26.881	1.00	46.48
ATOM	2028	CB	PHE	270	52.532	30.926	27.754	1.00	47.64
ATOM	2029	CG	PHE	270	52.853	30.875	29.221	1.00	47.84
ATOM	2030	CD1	PHE	270	53.395	31.978	29.865	1.00	49.86
ATOM	2031	CD2	PHE	270	52.604	29.727	29.962	1.00	50.22
ATOM	2032	CE1	PHE	270	53.682	31.941	31.234	1.00	51.58
ATOM	2033	CE2	PHE	270	52.888	29.679	31.326	1.00	50.74
ATOM	2034	CZ	PHE	270	53.427	30.791	31.963	1.00	50.30
ATOM	2035	C	PHE	270	54.902	30.433	27.152	1.00	45.41
ATOM	2036	O	PHE	270	54.750	29.220	27.261	1.00	45.07
ATOM	2037	N	GLY	271	56.083	31.024	27.261	1.00	45.52
ATOM	2038	CA	GLY	271	57.263	30.217	27.475	1.00	46.26
ATOM	2039	C	GLY	271	57.451	29.372	26.227	1.00	46.08
ATOM	2040	O	GLY	271	57.336	29.881	25.113	1.00	47.07
ATOM	2041	N	ALA	272	57.711	28.081	26.401	1.00	45.01
ATOM	2042	CA	ALA	272	57.910	27.207	25.262	1.00	44.35
ATOM	2043	CB	ALA	272	59.112	26.288	25.503	1.00	42.29
ATOM	2044	C	ALA	272	56.671	26.382	24.970	1.00	45.01
ATOM	2045	O	ALA	272	56.778	25.213	24.595	1.00	46.73
ATOM	2046	N	SER	273	55.493	26.973	25.134	1.00	44.94
ATOM	2047	CA	SER	273	54.278	26.216	24.855	1.00	47.72
ATOM	2048	CB	SER	273	53.795	25.497	26.120	1.00	48.16
ATOM	2049	OG	SER	273	53.297	26.428	27.055	1.00	53.37
ATOM	2050	C	SER	273	53.141	27.053	24.283	1.00	46.71
ATOM	2051	O	SER	273	53.121	28.271	24.435	1.00	44.26
ATOM	2052	N	CYS	274	52.210	26.378	23.608	1.00	45.77
ATOM	2053	CA	CYS	274	51.050	27.039	23.025	1.00	47.39
ATOM	2054	C	CYS	274	49.870	26.777	23.947	1.00	47.37
ATOM	2055	O	CYS	274	49.494	25.631	24.163	1.00	49.49
ATOM	2056	CB	CYS	274	50.735	26.476	21.639	1.00	47.43
ATOM	2057	SG	CYS	274	52.155	26.421	20.504	1.00	46.90
ATOM	2058	N	VAL	275	49.287	27.838	24.486	1.00	46.52
ATOM	2059	CA	VAL	275	48.168	27.690	25.403	1.00	46.86
ATOM	2060	CB	VAL	275	48.516	28.276	26.771	1.00	44.33
ATOM	2061	CG1	VAL	275	49.818	27.687	27.253	1.00	43.46
ATOM	2062	CG2	VAL	275	48.630	29.783	26.669	1.00	44.17
ATOM	2063	C	VAL	275	46.937	28.401	24.879	1.00	47.21
ATOM	2064	O	VAL	275	47.047	29.367	24.130	1.00	48.64
ATOM	2065	N	THR	276	45.768	27.925	25.291	1.00	47.78
ATOM	2066	CA	THR	276	44.497	28.509	24.864	1.00	47.96
ATOM	2067	CB	THR	276	43.337	27.562	25.180	1.00	48.33
ATOM	2068	OG1	THR	276	43.221	27.419	26.603	1.00	47.75
ATOM	2069	CG2	THR	276	43.592	26.188	24.555	1.00	47.06
ATOM	2070	C	THR	276	44.227	29.841	25.554	1.00	47.72

ATOM	2071	O	THR	276	43.563	30.710	25.005	1.00	47.53
ATOM	2072	N	ALA	277	44.743	29.990	26.768	1.00	48.65
ATOM	2073	CA	ALA	277	44.558	31.217	27.529	1.00	48.95
ATOM	2074	CB	ALA	277	43.339	31.091	28.434	1.00	49.82
ATOM	2075	C	ALA	277	45.788	31.497	28.371	1.00	48.96
ATOM	2076	O	ALA	277	46.396	30.572	28.921	1.00	48.47
ATOM	2077	N	CYS	278	46.157	32.771	28.472	1.00	49.32
ATOM	2078	CA	CYS	278	47.314	33.146	29.281	1.00	50.33
ATOM	2079	C	CYS	278	47.017	32.867	30.753	1.00	51.58
ATOM	2080	O	CYS	278	45.878	33.010	31.205	1.00	51.96
ATOM	2081	CB	CYS	278	47.650	34.626	29.095	1.00	46.73
ATOM	2082	SG	CYS	278	48.295	35.016	27.442	1.00	45.43
ATOM	2083	N	PRO	279	48.033	32.440	31.517	1.00	52.20
ATOM	2084	CD	PRO	279	49.389	32.030	31.107	1.00	53.86
ATOM	2085	CA	PRO	279	47.807	32.159	32.936	1.00	51.15
ATOM	2086	CB	PRO	279	49.062	31.390	33.343	1.00	51.40
ATOM	2087	CG	PRO	279	50.119	31.958	32.442	1.00	53.87
ATOM	2088	C	PRO	279	47.590	33.422	33.770	1.00	50.59
ATOM	2089	O	PRO	279	47.843	34.543	33.320	1.00	48.69
ATOM	2090	N	TYR	280	47.118	33.222	34.995	1.00	50.86
ATOM	2091	CA	TYR	280	46.841	34.318	35.905	1.00	49.82
ATOM	2092	CB	TYR	280	46.464	33.784	37.284	1.00	48.50
ATOM	2093	CG	TYR	280	45.914	34.859	38.180	1.00	48.40
ATOM	2094	CD1	TYR	280	44.638	35.374	37.970	1.00	49.04
ATOM	2095	CE1	TYR	280	44.144	36.418	38.747	1.00	49.87
ATOM	2096	CD2	TYR	280	46.689	35.413	39.194	1.00	48.78
ATOM	2097	CE2	TYR	280	46.206	36.459	39.979	1.00	50.12
ATOM	2098	CZ	TYR	280	44.933	36.957	39.747	1.00	50.73
ATOM	2099	OH	TYR	280	44.448	37.995	40.512	1.00	53.36
ATOM	2100	C	TYR	280	47.991	35.297	36.066	1.00	50.72
ATOM	2101	O	TYR	280	49.149	34.899	36.210	1.00	50.74
ATOM	2102	N	ASN	281	47.637	36.579	36.043	1.00	50.37
ATOM	2103	CA	ASN	281	48.562	37.690	36.219	1.00	51.25
ATOM	2104	CB	ASN	281	49.495	37.430	37.413	1.00	51.06
ATOM	2105	CG	ASN	281	49.975	38.723	38.068	1.00	51.36
ATOM	2106	OD1	ASN	281	49.221	39.689	38.171	1.00	51.17
ATOM	2107	ND2	ASN	281	51.220	38.739	38.526	1.00	51.60
ATOM	2108	C	ASN	281	49.379	38.071	34.989	1.00	51.58
ATOM	2109	O	ASN	281	50.151	39.036	35.027	1.00	50.94
ATOM	2110	N	TYR	282	49.211	37.326	33.902	1.00	51.57
ATOM	2111	CA	TYR	282	49.927	37.644	32.671	1.00	52.72
ATOM	2112	CB	TYR	282	50.364	36.368	31.948	1.00	52.57
ATOM	2113	CG	TYR	282	51.685	35.802	32.430	1.00	53.88
ATOM	2114	CD1	TYR	282	51.791	35.168	33.670	1.00	54.63
ATOM	2115	CE1	TYR	282	53.020	34.658	34.121	1.00	53.76
ATOM	2116	CD2	TYR	282	52.838	35.915	31.647	1.00	53.83
ATOM	2117	CE2	TYR	282	54.064	35.413	32.085	1.00	53.98
ATOM	2118	CZ	TYR	282	54.151	34.786	33.321	1.00	54.93
ATOM	2119	OH	TYR	282	55.363	34.284	33.751	1.00	54.27
ATOM	2120	C	TYR	282	49.061	38.495	31.742	1.00	53.12
ATOM	2121	O	TYR	282	47.845	38.578	31.904	1.00	51.51
ATOM	2122	N	LEU	283	49.699	39.132	30.770	1.00	54.89
ATOM	2123	CA	LEU	283	48.993	39.976	29.820	1.00	56.63
ATOM	2124	CB	LEU	283	49.729	41.311	29.671	1.00	58.42
ATOM	2125	CG	LEU	283	49.807	42.232	30.900	1.00	59.48
ATOM	2126	CD1	LEU	283	50.883	43.288	30.699	1.00	59.69
ATOM	2127	CD2	LEU	283	48.461	42.892	31.133	1.00	60.34
ATOM	2128	C	LEU	283	48.875	39.299	28.459	1.00	57.32
ATOM	2129	O	LEU	283	49.858	38.793	27.921	1.00	58.54
ATOM	2130	N	SER	284	47.663	39.273	27.913	1.00	58.71
ATOM	2131	CA	SER	284	47.422	38.681	26.600	1.00	59.30

ATOM	2132	CB	SER	284	45.977	38.197	26.481	1.00	58.31
ATOM	2133	OG	SER	284	45.749	37.090	27.340	1.00	58.17
ATOM	2134	C	SER	284	47.688	39.795	25.608	1.00	60.28
ATOM	2135	O	SER	284	47.313	40.939	25.855	1.00	60.43
ATOM	2136	N	THR	285	48.332	39.476	24.490	1.00	61.69
ATOM	2137	CA	THR	285	48.660	40.506	23.514	1.00	62.74
ATOM	2138	CB	THR	285	50.177	40.574	23.288	1.00	61.20
ATOM	2139	OG1	THR	285	50.617	39.392	22.605	1.00	60.25
ATOM	2140	CG2	THR	285	50.893	40.683	24.616	1.00	59.34
ATOM	2141	C	THR	285	47.997	40.382	22.155	1.00	65.35
ATOM	2142	O	THR	285	47.310	39.405	21.863	1.00	66.92
ATOM	2143	N	ASP	286	48.217	41.401	21.328	1.00	68.96
ATOM	2144	CA	ASP	286	47.680	41.456	19.974	1.00	70.35
ATOM	2145	CB	ASP	286	48.064	42.779	19.292	1.00	73.32
ATOM	2146	CG	ASP	286	47.489	44.000	19.991	1.00	75.72
ATOM	2147	OD1	ASP	286	46.253	44.191	19.922	1.00	75.54
ATOM	2148	OD2	ASP	286	48.276	44.763	20.603	1.00	76.45
ATOM	2149	C	ASP	286	48.318	40.325	19.191	1.00	70.06
ATOM	2150	O	ASP	286	47.648	39.581	18.467	1.00	70.44
ATOM	2151	N	VAL	287	49.631	40.210	19.356	1.00	68.31
ATOM	2152	CA	VAL	287	50.420	39.212	18.655	1.00	66.57
ATOM	2153	CB	VAL	287	51.900	39.626	18.622	1.00	68.51
ATOM	2154	CG1	VAL	287	52.583	38.997	17.402	1.00	70.27
ATOM	2155	CG2	VAL	287	52.016	41.147	18.609	1.00	67.05
ATOM	2156	C	VAL	287	50.330	37.807	19.237	1.00	64.30
ATOM	2157	O	VAL	287	51.238	36.999	19.048	1.00	64.78
ATOM	2158	N	GLY	288	49.247	37.522	19.953	1.00	62.01
ATOM	2159	CA	GLY	288	49.056	36.201	20.533	1.00	59.45
ATOM	2160	C	GLY	288	50.131	35.683	21.476	1.00	57.09
ATOM	2161	O	GLY	288	50.586	34.542	21.348	1.00	55.74
ATOM	2162	N	SER	289	50.546	36.509	22.426	1.00	55.12
ATOM	2163	CA	SER	289	51.557	36.082	23.381	1.00	55.42
ATOM	2164	CB	SER	289	52.903	36.772	23.091	1.00	55.58
ATOM	2165	OG	SER	289	52.827	38.181	23.246	1.00	54.26
ATOM	2166	C	SER	289	51.119	36.373	24.815	1.00	54.82
ATOM	2167	O	SER	289	50.156	37.109	25.051	1.00	52.55
ATOM	2168	N	CYS	290	51.822	35.771	25.768	1.00	54.19
ATOM	2169	CA	CYS	290	51.535	35.989	27.176	1.00	54.40
ATOM	2170	C	CYS	290	52.756	36.694	27.740	1.00	56.69
ATOM	2171	O	CYS	290	53.846	36.119	27.849	1.00	56.87
ATOM	2172	CB	CYS	290	51.286	34.661	27.884	1.00	51.20
ATOM	2173	SG	CYS	290	49.861	33.745	27.217	1.00	48.94
ATOM	2174	N	THR	291	52.576	37.957	28.088	1.00	58.96
ATOM	2175	CA	THR	291	53.692	38.732	28.586	1.00	62.71
ATOM	2176	CB	THR	291	54.214	39.664	27.492	1.00	62.87
ATOM	2177	OG1	THR	291	55.427	40.284	27.929	1.00	67.19
ATOM	2178	CG2	THR	291	53.181	40.738	27.185	1.00	62.81
ATOM	2179	C	THR	291	53.350	39.570	29.800	1.00	64.32
ATOM	2180	O	THR	291	52.178	39.807	30.105	1.00	64.63
ATOM	2181	N	LEU	292	54.396	40.024	30.482	1.00	65.88
ATOM	2182	CA	LEU	292	54.249	40.857	31.665	1.00	67.54
ATOM	2183	CB	LEU	292	55.361	40.537	32.663	1.00	64.73
ATOM	2184	CG	LEU	292	55.548	39.042	32.941	1.00	65.08
ATOM	2185	CD1	LEU	292	56.703	38.835	33.898	1.00	64.62
ATOM	2186	CD2	LEU	292	54.270	38.454	33.512	1.00	64.78
ATOM	2187	C	LEU	292	54.300	42.338	31.280	1.00	69.22
ATOM	2188	O	LEU	292	53.964	43.204	32.085	1.00	70.92
ATOM	2189	N	VAL	293	54.707	42.625	30.047	1.00	71.80
ATOM	2190	CA	VAL	293	54.803	44.003	29.577	1.00	75.12
ATOM	2191	CB	VAL	293	56.269	44.492	29.586	1.00	75.39
ATOM	2192	CG1	VAL	293	56.303	46.012	29.559	1.00	75.24

ATOM	2193	CG2	VAL	293	57.009	43.945	30.809	1.00	74.43
ATOM	2194	C	VAL	293	54.264	44.109	28.155	1.00	77.87
ATOM	2195	O	VAL	293	54.600	43.294	27.303	1.00	78.41
ATOM	2196	N	CYS	294	53.441	45.120	27.899	1.00	81.86
ATOM	2197	CA	CYS	294	52.840	45.315	26.581	1.00	87.12
ATOM	2198	C	CYS	294	53.783	45.780	25.455	1.00	91.22
ATOM	2199	O	CYS	294	54.965	46.052	25.685	1.00	91.41
ATOM	2200	CB	CYS	294	51.676	46.299	26.685	1.00	86.96
ATOM	2201	SG	CYS	294	50.194	45.704	27.562	1.00	88.97
ATOM	2202	N	PRO	295	53.258	45.854	24.208	1.00	95.10
ATOM	2203	CD	PRO	295	52.018	45.149	23.830	1.00	96.29
ATOM	2204	CA	PRO	295	53.979	46.276	22.996	1.00	97.21
ATOM	2205	CB	PRO	295	53.069	45.788	21.863	1.00	96.88
ATOM	2206	CG	PRO	295	52.360	44.617	22.463	1.00	96.55
ATOM	2207	C	PRO	295	54.246	47.781	22.887	1.00	98.82
ATOM	2208	O	PRO	295	53.619	48.585	23.581	1.00	98.72
ATOM	2209	N	LEU	296	55.172	48.137	21.992	1.00	100.53
ATOM	2210	CA	LEU	296	55.571	49.524	21.731	1.00	102.46
ATOM	2211	CB	LEU	296	55.670	49.784	20.223	1.00	103.54
ATOM	2212	CG	LEU	296	56.912	49.335	19.452	1.00	104.08
ATOM	2213	CD1	LEU	296	56.713	49.602	17.963	1.00	103.26
ATOM	2214	CD2	LEU	296	58.138	50.078	19.974	1.00	103.86
ATOM	2215	C	LEU	296	54.635	50.560	22.321	1.00	103.21
ATOM	2216	O	LEU	296	54.820	51.017	23.449	1.00	103.65
ATOM	2217	N	HIS	297	53.629	50.933	21.539	1.00	104.02
ATOM	2218	CA	HIS	297	52.665	51.925	21.973	1.00	104.87
ATOM	2219	CB	HIS	297	52.446	52.953	20.871	1.00	105.33
ATOM	2220	C	HIS	297	51.338	51.301	22.387	1.00	105.28
ATOM	2221	O	HIS	297	50.342	52.005	22.515	1.00	105.58
ATOM	2222	N	ASP	298	51.323	49.984	22.585	1.00	105.05
ATOM	2223	CA	ASP	298	50.108	49.290	23.019	1.00	104.04
ATOM	2224	CB	ASP	298	50.140	47.815	22.602	1.00	103.55
ATOM	2225	CG	ASP	298	49.793	47.659	21.238	1.00	102.45
ATOM	2226	C	ASP	298	50.009	49.395	24.538	1.00	103.29
ATOM	2227	O	ASP	298	51.029	49.358	25.229	1.00	103.87
ATOM	2228	N	GLN	299	48.794	49.527	25.064	1.00	101.99
ATOM	2229	CA	GLN	299	48.634	49.649	26.506	1.00	101.04
ATOM	2230	CB	GLN	299	48.371	51.107	26.866	1.00	101.54
ATOM	2231	CG	GLN	299	49.451	52.031	26.331	1.00	102.81
ATOM	2232	CD	GLN	299	49.618	53.289	27.159	1.00	104.15
ATOM	2233	OE1	GLN	299	48.641	53.969	27.483	1.00	104.75
ATOM	2234	NE2	GLN	299	50.865	53.614	27.498	1.00	103.49
ATOM	2235	C	GLN	299	47.576	48.747	27.142	1.00	100.08
ATOM	2236	O	GLN	299	46.638	48.293	26.483	1.00	100.27
ATOM	2237	N	GLU	300	47.749	48.501	28.438	1.00	98.05
ATOM	2238	CA	GLU	300	46.867	47.635	29.215	1.00	96.41
ATOM	2239	CB	GLU	300	47.407	47.512	30.641	1.00	95.18
ATOM	2240	CG	GLU	300	48.771	46.846	30.711	1.00	93.52
ATOM	2241	CD	GLU	300	49.335	46.801	32.111	1.00	91.95
ATOM	2242	OE1	GLU	300	48.591	46.407	33.031	1.00	92.20
ATOM	2243	OE2	GLU	300	50.523	47.148	32.291	1.00	90.84
ATOM	2244	C	GLU	300	45.407	48.061	29.261	1.00	95.94
ATOM	2245	O	GLU	300	45.092	49.242	29.346	1.00	95.78
ATOM	2246	N	VAL	301	44.519	47.074	29.209	1.00	95.93
ATOM	2247	CA	VAL	301	43.081	47.307	29.251	1.00	96.56
ATOM	2248	CB	VAL	301	42.452	47.153	27.857	1.00	96.60
ATOM	2249	CG1	VAL	301	40.966	47.486	27.915	1.00	96.39
ATOM	2250	CG2	VAL	301	43.174	48.049	26.866	1.00	96.93
ATOM	2251	C	VAL	301	42.432	46.290	30.183	1.00	97.30
ATOM	2252	O	VAL	301	42.285	45.118	29.833	1.00	96.75
ATOM	2253	N	THR	302	42.038	46.747	31.367	1.00	98.44

ATOM	2254	CA	THR	302	41.426	45.875	32.360	1.00 99.64
ATOM	2255	CB	THR	302	41.483	46.500	33.767	1.00 99.04
ATOM	2256	OG1	THR	302	42.818	46.934	34.050	1.00 98.39
ATOM	2257	CG2	THR	302	41.053	45.484	34.812	1.00 97.82
ATOM	2258	C	THR	302	39.972	45.554	32.063	1.00101.32
ATOM	2259	O	THR	302	39.126	46.448	32.038	1.00101.86
ATOM	2260	N	ALA	303	39.687	44.275	31.836	1.00103.31
ATOM	2261	CA	ALA	303	38.322	43.828	31.583	1.00105.07
ATOM	2262	CB	ALA	303	38.320	42.572	30.714	1.00104.35
ATOM	2263	C	ALA	303	37.733	43.530	32.961	1.00106.78
ATOM	2264	O	ALA	303	38.480	43.314	33.918	1.00106.64
ATOM	2265	N	GLU	304	36.406	43.529	33.065	1.00108.54
ATOM	2266	CA	GLU	304	35.729	43.274	34.339	1.00109.78
ATOM	2267	CB	GLU	304	34.251	42.959	34.107	1.00110.34
ATOM	2268	CG	GLU	304	33.458	44.049	33.413	1.00110.81
ATOM	2269	CD	GLU	304	31.973	43.724	33.360	1.00111.13
ATOM	2270	OE1	GLU	304	31.614	42.628	32.869	1.00110.92
ATOM	2271	OE2	GLU	304	31.167	44.567	33.814	1.00111.09
ATOM	2272	C	GLU	304	36.345	42.118	35.117	1.00110.69
ATOM	2273	O	GLU	304	36.803	42.290	36.251	1.00111.35
ATOM	2274	N	ASP	305	36.338	40.939	34.500	1.00110.93
ATOM	2275	CA	ASP	305	36.874	39.725	35.109	1.00110.67
ATOM	2276	CB	ASP	305	36.698	38.541	34.144	1.00110.84
ATOM	2277	CG	ASP	305	37.331	38.790	32.782	1.00111.14
ATOM	2278	OD1	ASP	305	37.777	39.927	32.519	1.00111.75
ATOM	2279	OD2	ASP	305	37.373	37.843	31.968	1.00111.02
ATOM	2280	C	ASP	305	38.336	39.826	35.559	1.00110.28
ATOM	2281	O	ASP	305	38.787	39.039	36.394	1.00110.13
ATOM	2282	N	GLY	306	39.074	40.789	35.013	1.00109.66
ATOM	2283	CA	GLY	306	40.467	40.948	35.395	1.00108.63
ATOM	2284	C	GLY	306	41.439	40.719	34.257	1.00107.62
ATOM	2285	O	GLY	306	42.580	41.180	34.305	1.00108.33
ATOM	2286	N	THR	307	40.992	40.003	33.231	1.00106.17
ATOM	2287	CA	THR	307	41.831	39.722	32.074	1.00104.19
ATOM	2288	CB	THR	307	41.062	38.924	31.004	1.00104.68
ATOM	2289	OG1	THR	307	40.574	37.703	31.574	1.00104.14
ATOM	2290	CG2	THR	307	41.971	38.606	29.823	1.00104.37
ATOM	2291	C	THR	307	42.300	41.026	31.442	1.00103.03
ATOM	2292	O	THR	307	41.551	41.672	30.708	1.00102.75
ATOM	2293	N	GLN	308	43.536	41.417	31.735	1.00101.57
ATOM	2294	CA	GLN	308	44.087	42.643	31.175	1.00100.15
ATOM	2295	CB	GLN	308	45.086	43.281	32.137	1.00 99.43
ATOM	2296	CG	GLN	308	44.471	43.874	33.385	1.00 99.19
ATOM	2297	CD	GLN	308	45.501	44.589	34.240	1.00100.05
ATOM	2298	OE1	GLN	308	46.469	43.983	34.697	1.00100.13
ATOM	2299	NE2	GLN	308	45.301	45.884	34.454	1.00100.28
ATOM	2300	C	GLN	308	44.784	42.338	29.860	1.00 99.59
ATOM	2301	O	GLN	308	45.744	41.570	29.820	1.00 99.52
ATOM	2302	N	ARG	309	44.288	42.938	28.783	1.00 98.88
ATOM	2303	CA	ARG	309	44.867	42.733	27.467	1.00 97.82
ATOM	2304	CB	ARG	309	43.767	42.612	26.407	1.00 97.73
ATOM	2305	CG	ARG	309	42.669	41.612	26.738	1.00 98.41
ATOM	2306	CD	ARG	309	41.374	42.306	27.164	1.00 99.02
ATOM	2307	NE	ARG	309	40.752	43.094	26.010	1.00 98.96
ATOM	2308	CZ	ARG	309	39.449	43.716	26.380	1.00 98.63
ATOM	2309	C	ARG	309	45.747	43.922	27.132	1.00 97.75
ATOM	2310	O	ARG	309	45.816	44.889	27.889	1.00 97.57
ATOM	2311	N	CYS	310	46.433	43.832	26.000	1.00 97.78
ATOM	2312	CA	CYS	310	47.282	44.915	25.527	1.00 97.65
ATOM	2313	C	CYS	310	46.661	45.373	24.214	1.00100.22
ATOM	2314	O	CYS	310	46.607	44.603	23.259	1.00101.04

ATOM	2315	CB	CYS	310	48.704	44.428	25.254	1.00 94.17
ATOM	2316	SG	CYS	310	49.711	43.939	26.685	1.00 88.15
ATOM	2317	N	GLU	311	46.185	46.613	24.162	1.00103.10
ATOM	2318	CA	GLU	311	45.573	47.134	22.942	1.00105.28
ATOM	2319	CB	GLU	311	44.196	47.730	23.254	1.00104.85
ATOM	2320	CG	GLU	311	43.048	46.757	23.046	1.00105.54
ATOM	2321	CD	GLU	311	41.703	47.337	23.442	1.00106.78
ATOM	2322	OE1	GLU	311	41.383	48.469	23.014	1.00107.43
ATOM	2323	OE2	GLU	311	40.960	46.654	24.178	1.00107.11
ATOM	2324	C	GLU	311	46.441	48.174	22.238	1.00106.82
ATOM	2325	O	GLU	311	47.365	48.729	22.832	1.00106.91
ATOM	2326	N	LYS	312	46.139	48.426	20.965	1.00108.60
ATOM	2327	CA	LYS	312	46.883	49.401	20.174	1.00109.53
ATOM	2328	CB	LYS	312	46.471	49.321	18.705	1.00109.04
ATOM	2329	C	LYS	312	46.625	50.799	20.719	1.00110.29
ATOM	2330	O	LYS	312	45.501	51.303	20.686	1.00110.37
ATOM	2331	N	CYS	313	47.683	51.414	21.227	1.00111.11
ATOM	2332	CA	CYS	313	47.609	52.749	21.796	1.00111.89
ATOM	2333	C	CYS	313	48.738	53.504	21.100	1.00112.43
ATOM	2334	O	CYS	313	49.352	54.408	21.664	1.00112.94
ATOM	2335	CB	CYS	313	47.847	52.650	23.308	1.00111.88
ATOM	2336	SG	CYS	313	47.192	53.962	24.389	1.00112.06
ATOM	2337	N	SER	314	49.008	53.097	19.863	0.01112.82
ATOM	2338	CA	SER	314	50.062	53.689	19.053	0.01113.18
ATOM	2339	CB	SER	314	50.033	53.096	17.650	0.01113.17
ATOM	2340	C	SER	314	49.953	55.202	18.979	0.01113.47
ATOM	2341	O	SER	314	50.797	55.926	19.509	0.01113.48
ATOM	2342	N	LYS	315	48.904	55.675	18.321	1.00113.74
ATOM	2343	CA	LYS	315	48.694	57.105	18.165	1.00114.23
ATOM	2344	CB	LYS	315	47.988	57.382	16.832	1.00114.86
ATOM	2345	CG	LYS	315	48.771	56.924	15.609	1.00114.98
ATOM	2346	CD	LYS	315	50.098	57.663	15.500	1.00114.63
ATOM	2347	CE	LYS	315	50.837	57.298	14.225	1.00114.17
ATOM	2348	NZ	LYS	315	52.118	58.046	14.103	1.00113.31
ATOM	2349	C	LYS	315	47.936	57.753	19.328	1.00113.77
ATOM	2350	O	LYS	315	48.546	58.446	20.144	1.00114.04
ATOM	2351	N	PRO	316	46.605	57.544	19.428	1.00113.20
ATOM	2352	CD	PRO	316	45.675	56.793	18.572	1.00112.87
ATOM	2353	CA	PRO	316	45.874	58.165	20.541	1.00112.47
ATOM	2354	CB	PRO	316	44.404	57.964	20.155	1.00112.47
ATOM	2355	CG	PRO	316	44.443	57.634	18.679	1.00112.56
ATOM	2356	C	PRO	316	46.213	57.433	21.836	1.00111.90
ATOM	2357	O	PRO	316	45.640	56.374	22.116	1.00112.00
ATOM	2358	N	CYS	317	47.132	57.984	22.627	1.00110.08
ATOM	2359	CA	CYS	317	47.515	57.312	23.862	1.00107.76
ATOM	2360	C	CYS	317	47.772	58.186	25.090	1.00105.03
ATOM	2361	O	CYS	317	48.751	58.935	25.145	1.00104.64
ATOM	2362	CB	CYS	317	48.735	56.431	23.602	1.00108.86
ATOM	2363	SG	CYS	317	48.819	55.102	24.827	1.00111.58
ATOM	2364	N	ALA	318	46.892	58.053	26.082	1.00101.44
ATOM	2365	CA	ALA	318	46.982	58.809	27.331	1.00 98.34
ATOM	2366	CB	ALA	318	45.746	58.546	28.185	1.00 97.94
ATOM	2367	C	ALA	318	48.241	58.464	28.122	1.00 95.80
ATOM	2368	O	ALA	318	48.574	57.291	28.293	1.00 95.52
ATOM	2369	N	ARG	319	48.930	59.493	28.609	1.00 92.64
ATOM	2370	CA	ARG	319	50.154	59.315	29.387	1.00 89.08
ATOM	2371	CB	ARG	319	50.795	60.680	29.692	1.00 90.56
ATOM	2372	CG	ARG	319	49.875	61.703	30.371	1.00 91.95
ATOM	2373	CD	ARG	319	49.847	61.586	31.899	1.00 92.71
ATOM	2374	NE	ARG	319	51.142	61.897	32.506	1.00 93.30
ATOM	2375	CZ	ARG	319	51.349	62.018	33.815	1.00 93.09

ATOM	2376	NH1	ARG	319	50.345	61.860	34.671	1.00	91.92
ATOM	2377	NH2	ARG	319	52.567	62.289	34.270	1.00	92.71
ATOM	2378	C	ARG	319	49.899	58.559	30.688	1.00	85.21
ATOM	2379	O	ARG	319	48.840	58.692	31.306	1.00	85.67
ATOM	2380	N	VAL	320	50.878	57.760	31.097	1.00	79.32
ATOM	2381	CA	VAL	320	50.754	56.986	32.323	1.00	72.87
ATOM	2382	CB	VAL	320	50.689	55.473	32.024	1.00	71.59
ATOM	2383	CG1	VAL	320	49.490	55.170	31.142	1.00	69.01
ATOM	2384	CG2	VAL	320	51.980	55.014	31.360	1.00	68.56
ATOM	2385	C	VAL	320	51.936	57.248	33.242	1.00	69.92
ATOM	2386	O	VAL	320	52.937	57.843	32.841	1.00	68.57
ATOM	2387	N	CYS	321	51.811	56.805	34.485	1.00	65.95
ATOM	2388	CA	CYS	321	52.882	56.973	35.449	1.00	62.47
ATOM	2389	C	CYS	321	53.787	55.748	35.418	1.00	60.43
ATOM	2390	O	CYS	321	53.364	54.654	35.785	1.00	59.95
ATOM	2391	CB	CYS	321	52.303	57.122	36.845	1.00	62.31
ATOM	2392	SG	CYS	321	51.145	58.507	37.041	1.00	60.91
ATOM	2393	N	TYR	322	55.021	55.925	34.966	1.00	58.69
ATOM	2394	CA	TYR	322	55.962	54.821	34.929	1.00	57.74
ATOM	2395	CB	TYR	322	56.921	54.951	33.747	1.00	60.17
ATOM	2396	CG	TYR	322	56.281	54.638	32.420	1.00	62.41
ATOM	2397	CD1	TYR	322	55.945	55.656	31.528	1.00	63.63
ATOM	2398	CE1	TYR	322	55.315	55.372	30.318	1.00	64.44
ATOM	2399	CD2	TYR	322	55.975	53.323	32.069	1.00	61.83
ATOM	2400	CE2	TYR	322	55.343	53.029	30.865	1.00	63.82
ATOM	2401	CZ	TYR	322	55.016	54.057	29.995	1.00	64.36
ATOM	2402	OH	TYR	322	54.374	53.778	28.813	1.00	64.79
ATOM	2403	C	TYR	322	56.749	54.830	36.224	1.00	56.52
ATOM	2404	O	TYR	322	57.066	55.892	36.754	1.00	57.52
ATOM	2405	N	GLY	323	57.062	53.646	36.737	1.00	54.51
ATOM	2406	CA	GLY	323	57.803	53.570	37.979	1.00	50.35
ATOM	2407	C	GLY	323	59.208	53.077	37.749	1.00	48.48
ATOM	2408	O	GLY	323	59.654	52.971	36.605	1.00	46.95
ATOM	2409	N	LEU	324	59.906	52.775	38.840	1.00	47.45
ATOM	2410	CA	LEU	324	61.271	52.287	38.755	1.00	46.55
ATOM	2411	CB	LEU	324	61.821	52.000	40.154	1.00	47.15
ATOM	2412	CG	LEU	324	61.766	53.157	41.170	1.00	48.69
ATOM	2413	CD1	LEU	324	62.424	52.736	42.484	1.00	48.11
ATOM	2414	CD2	LEU	324	62.477	54.386	40.606	1.00	48.58
ATOM	2415	C	LEU	324	61.301	51.030	37.897	1.00	46.35
ATOM	2416	O	LEU	324	60.404	50.189	37.977	1.00	45.07
ATOM	2417	N	GLY	325	62.329	50.932	37.058	1.00	47.27
ATOM	2418	CA	GLY	325	62.486	49.793	36.178	1.00	47.12
ATOM	2419	C	GLY	325	61.836	50.005	34.824	1.00	49.50
ATOM	2420	O	GLY	325	62.022	49.204	33.904	1.00	49.51
ATOM	2421	N	MET	326	61.073	51.085	34.687	1.00	50.15
ATOM	2422	CA	MET	326	60.395	51.357	33.424	1.00	51.67
ATOM	2423	CB	MET	326	58.881	51.323	33.634	1.00	52.43
ATOM	2424	CG	MET	326	58.332	49.938	33.912	1.00	54.09
ATOM	2425	SD	MET	326	58.490	48.857	32.476	1.00	58.51
ATOM	2426	CE	MET	326	56.995	49.301	31.579	1.00	57.02
ATOM	2427	C	MET	326	60.790	52.676	32.764	1.00	52.23
ATOM	2428	O	MET	326	61.170	53.637	33.438	1.00	51.49
ATOM	2429	N	GLU	327	60.693	52.701	31.436	1.00	53.25
ATOM	2430	CA	GLU	327	61.017	53.875	30.624	1.00	54.18
ATOM	2431	CB	GLU	327	59.795	54.790	30.529	1.00	55.32
ATOM	2432	CG	GLU	327	58.654	54.175	29.738	1.00	58.20
ATOM	2433	CD	GLU	327	59.108	53.717	28.368	1.00	60.14
ATOM	2434	OE1	GLU	327	59.744	54.531	27.673	1.00	62.16
ATOM	2435	OE2	GLU	327	58.833	52.557	27.981	1.00	60.33
ATOM	2436	C	GLU	327	62.232	54.669	31.099	1.00	53.77

ATOM	2437	O	GLU	327	63.343	54.135	31.155	1.00	53.63
ATOM	2438	N	HIS	328	62.034	55.939	31.436	1.00	53.71
ATOM	2439	CA	HIS	328	63.160	56.741	31.882	1.00	54.74
ATOM	2440	CB	HIS	328	62.815	58.240	31.910	1.00	54.63
ATOM	2441	CG	HIS	328	61.685	58.603	32.817	1.00	53.25
ATOM	2442	CD2	HIS	328	61.656	59.345	33.950	1.00	53.62
ATOM	2443	ND1	HIS	328	60.378	58.240	32.565	1.00	53.71
ATOM	2444	CE1	HIS	328	59.593	58.745	33.501	1.00	53.04
ATOM	2445	NE2	HIS	328	60.343	59.420	34.353	1.00	55.48
ATOM	2446	C	HIS	328	63.707	56.311	33.223	1.00	55.75
ATOM	2447	O	HIS	328	64.892	56.498	33.488	1.00	57.58
ATOM	2448	N	LEU	329	62.862	55.709	34.058	1.00	56.08
ATOM	2449	CA	LEU	329	63.291	55.261	35.384	1.00	55.37
ATOM	2450	CB	LEU	329	62.110	55.322	36.362	1.00	54.06
ATOM	2451	CG	LEU	329	61.512	56.725	36.547	1.00	54.58
ATOM	2452	CD1	LEU	329	60.185	56.665	37.287	1.00	53.35
ATOM	2453	CD2	LEU	329	62.513	57.587	37.296	1.00	53.68
ATOM	2454	C	LEU	329	63.884	53.855	35.374	1.00	55.48
ATOM	2455	O	LEU	329	64.213	53.313	36.426	1.00	56.56
ATOM	2456	N	ARG	330	64.035	53.278	34.185	1.00	54.51
ATOM	2457	CA	ARG	330	64.567	51.929	34.042	1.00	55.09
ATOM	2458	CB	ARG	330	64.811	51.610	32.558	1.00	57.19
ATOM	2459	CG	ARG	330	65.548	50.287	32.322	1.00	61.45
ATOM	2460	CD	ARG	330	65.206	49.616	30.982	1.00	67.13
ATOM	2461	NE	ARG	330	65.373	50.493	29.817	1.00	72.58
ATOM	2462	CZ	ARG	330	64.371	51.106	29.183	1.00	75.31
ATOM	2463	NH1	ARG	330	63.118	50.940	29.595	1.00	75.51
ATOM	2464	NH2	ARG	330	64.616	51.887	28.132	1.00	76.41
ATOM	2465	C	ARG	330	65.825	51.598	34.841	1.00	54.88
ATOM	2466	O	ARG	330	66.009	50.454	35.257	1.00	55.54
ATOM	2467	N	GLU	331	66.693	52.581	35.065	1.00	55.30
ATOM	2468	CA	GLU	331	67.935	52.323	35.798	1.00	52.86
ATOM	2469	CB	GLU	331	69.144	52.838	35.001	1.00	54.33
ATOM	2470	CG	GLU	331	69.397	52.157	33.653	1.00	56.11
ATOM	2471	CD	GLU	331	68.403	52.567	32.570	1.00	58.11
ATOM	2472	OE1	GLU	331	67.824	53.674	32.682	1.00	58.17
ATOM	2473	OE2	GLU	331	68.220	51.793	31.596	1.00	56.57
ATOM	2474	C	GLU	331	67.970	52.930	37.196	1.00	51.54
ATOM	2475	O	GLU	331	68.918	52.702	37.951	1.00	50.00
ATOM	2476	N	VAL	332	66.950	53.717	37.530	1.00	51.04
ATOM	2477	CA	VAL	332	66.871	54.350	38.844	1.00	51.96
ATOM	2478	CB	VAL	332	65.764	55.414	38.886	1.00	51.13
ATOM	2479	CG1	VAL	332	65.749	56.088	40.250	1.00	49.43
ATOM	2480	CG2	VAL	332	65.984	56.435	37.780	1.00	48.05
ATOM	2481	C	VAL	332	66.574	53.285	39.892	1.00	53.80
ATOM	2482	O	VAL	332	65.620	52.518	39.756	1.00	54.40
ATOM	2483	N	ARG	333	67.384	53.236	40.942	1.00	56.37
ATOM	2484	CA	ARG	333	67.189	52.219	41.966	1.00	59.44
ATOM	2485	CB	ARG	333	68.532	51.602	42.370	1.00	60.59
ATOM	2486	CG	ARG	333	69.412	52.502	43.215	1.00	66.44
ATOM	2487	CD	ARG	333	69.823	53.776	42.474	1.00	71.63
ATOM	2488	NE	ARG	333	70.882	54.496	43.184	1.00	76.84
ATOM	2489	CZ	ARG	333	72.081	53.985	43.470	1.00	79.39
ATOM	2490	NH1	ARG	333	72.387	52.739	43.107	1.00	79.11
ATOM	2491	NH2	ARG	333	72.982	54.720	44.116	1.00	79.77
ATOM	2492	C	ARG	333	66.455	52.675	43.220	1.00	58.57
ATOM	2493	O	ARG	333	66.384	51.916	44.183	1.00	59.16
ATOM	2494	N	ALA	334	65.902	53.888	43.212	1.00	57.03
ATOM	2495	CA	ALA	334	65.191	54.383	44.388	1.00	55.85
ATOM	2496	CB	ALA	334	66.177	54.615	45.519	1.00	52.63
ATOM	2497	C	ALA	334	64.362	55.644	44.175	1.00	56.09

ATOM	2498	O	ALA	334	64.617	56.436	43.272	1.00	56.32
ATOM	2499	N	VAL	335	63.355	55.820	45.024	1.00	57.27
ATOM	2500	CA	VAL	335	62.498	56.997	44.965	1.00	57.41
ATOM	2501	CB	VAL	335	61.114	56.714	45.602	1.00	57.83
ATOM	2502	CG1	VAL	335	60.357	58.006	45.828	1.00	56.01
ATOM	2503	CG2	VAL	335	60.310	55.792	44.694	1.00	56.93
ATOM	2504	C	VAL	335	63.222	58.083	45.748	1.00	58.30
ATOM	2505	O	VAL	335	63.682	57.852	46.871	1.00	58.06
ATOM	2506	N	THR	336	63.342	59.263	45.149	1.00	59.37
ATOM	2507	CA	THR	336	64.039	60.365	45.800	1.00	59.83
ATOM	2508	CB	THR	336	65.463	60.511	45.266	1.00	58.36
ATOM	2509	OG1	THR	336	65.402	61.041	43.939	1.00	59.09
ATOM	2510	CG2	THR	336	66.175	59.159	45.232	1.00	57.89
ATOM	2511	C	THR	336	63.334	61.687	45.542	1.00	61.53
ATOM	2512	O	THR	336	62.333	61.747	44.822	1.00	62.10
ATOM	2513	N	SER	337	63.876	62.747	46.136	1.00	62.16
ATOM	2514	CA	SER	337	63.337	64.091	45.977	1.00	61.32
ATOM	2515	CB	SER	337	64.154	65.077	46.807	1.00	60.42
ATOM	2516	OG	SER	337	64.087	64.756	48.183	1.00	62.18
ATOM	2517	C	SER	337	63.413	64.485	44.508	1.00	61.14
ATOM	2518	O	SER	337	62.650	65.334	44.035	1.00	59.75
ATOM	2519	N	ALA	338	64.336	63.846	43.796	1.00	61.33
ATOM	2520	CA	ALA	338	64.556	64.114	42.381	1.00	62.09
ATOM	2521	CB	ALA	338	65.957	63.649	41.985	1.00	61.47
ATOM	2522	C	ALA	338	63.515	63.486	41.453	1.00	62.48
ATOM	2523	O	ALA	338	63.526	63.747	40.247	1.00	63.76
ATOM	2524	N	ASN	339	62.624	62.658	41.996	1.00	61.25
ATOM	2525	CA	ASN	339	61.597	62.017	41.173	1.00	60.09
ATOM	2526	CB	ASN	339	62.092	60.652	40.672	1.00	58.96
ATOM	2527	CG	ASN	339	62.569	59.741	41.801	1.00	59.46
ATOM	2528	OD1	ASN	339	61.845	59.486	42.755	1.00	60.66
ATOM	2529	ND2	ASN	339	63.791	59.239	41.682	1.00	59.53
ATOM	2530	C	ASN	339	60.248	61.851	41.873	1.00	60.07
ATOM	2531	O	ASN	339	59.242	61.546	41.239	1.00	60.23
ATOM	2532	N	ILE	340	60.228	62.070	43.180	1.00	59.91
ATOM	2533	CA	ILE	340	59.011	61.920	43.958	1.00	61.02
ATOM	2534	CB	ILE	340	59.236	62.413	45.417	1.00	61.44
ATOM	2535	CG2	ILE	340	59.850	63.807	45.413	1.00	60.10
ATOM	2536	CG1	ILE	340	57.918	62.368	46.196	1.00	60.95
ATOM	2537	CD1	ILE	340	57.392	60.970	46.422	1.00	59.08
ATOM	2538	C	ILE	340	57.785	62.617	43.359	1.00	61.93
ATOM	2539	O	ILE	340	56.683	62.056	43.362	1.00	61.85
ATOM	2540	N	GLN	341	57.966	63.830	42.843	1.00	63.02
ATOM	2541	CA	GLN	341	56.847	64.575	42.268	1.00	63.53
ATOM	2542	CB	GLN	341	57.258	66.018	41.958	1.00	65.29
ATOM	2543	CG	GLN	341	56.910	67.016	43.070	1.00	66.87
ATOM	2544	CD	GLN	341	55.411	67.055	43.386	1.00	67.11
ATOM	2545	OE1	GLN	341	54.579	67.344	42.516	1.00	66.49
ATOM	2546	NE2	GLN	341	55.066	66.762	44.636	1.00	65.92
ATOM	2547	C	GLN	341	56.238	63.944	41.025	1.00	63.04
ATOM	2548	O	GLN	341	55.080	64.204	40.702	1.00	64.33
ATOM	2549	N	GLU	342	57.011	63.112	40.333	1.00	60.92
ATOM	2550	CA	GLU	342	56.528	62.450	39.126	1.00	59.81
ATOM	2551	CB	GLU	342	57.655	61.627	38.490	1.00	60.69
ATOM	2552	CG	GLU	342	58.774	62.431	37.861	1.00	61.90
ATOM	2553	CD	GLU	342	59.878	61.543	37.304	1.00	64.99
ATOM	2554	OE1	GLU	342	59.547	60.520	36.660	1.00	65.22
ATOM	2555	OE2	GLU	342	61.073	61.871	37.498	1.00	65.92
ATOM	2556	C	GLU	342	55.324	61.529	39.377	1.00	58.93
ATOM	2557	O	GLU	342	54.658	61.093	38.431	1.00	59.33
ATOM	2558	N	PHE	343	55.031	61.237	40.641	1.00	56.77

ATOM	2559	CA	PHE	343	53.928	60.332	40.944	1.00	54.80
ATOM	2560	CB	PHE	343	54.373	59.303	41.980	1.00	51.72
ATOM	2561	CG	PHE	343	55.591	58.538	41.565	1.00	48.42
ATOM	2562	CD1	PHE	343	56.796	58.704	42.238	1.00	46.96
ATOM	2563	CD2	PHE	343	55.548	57.689	40.467	1.00	47.13
ATOM	2564	CE1	PHE	343	57.940	58.040	41.824	1.00	44.73
ATOM	2565	CE2	PHE	343	56.688	57.019	40.045	1.00	46.48
ATOM	2566	CZ	PHE	343	57.889	57.197	40.727	1.00	44.96
ATOM	2567	C	PHE	343	52.660	61.009	41.399	1.00	54.34
ATOM	2568	O	PHE	343	51.655	60.344	41.662	1.00	53.92
ATOM	2569	N	ALA	344	52.704	62.333	41.483	1.00	53.73
ATOM	2570	CA	ALA	344	51.541	63.107	41.894	1.00	52.84
ATOM	2571	CB	ALA	344	51.797	64.577	41.640	1.00	52.20
ATOM	2572	C	ALA	344	50.286	62.658	41.140	1.00	53.05
ATOM	2573	O	ALA	344	50.287	62.559	39.910	1.00	52.61
ATOM	2574	N	GLY	345	49.222	62.374	41.888	1.00	53.32
ATOM	2575	CA	GLY	345	47.965	61.968	41.283	1.00	53.54
ATOM	2576	C	GLY	345	47.972	60.678	40.482	1.00	55.19
ATOM	2577	O	GLY	345	47.063	60.422	39.682	1.00	54.90
ATOM	2578	N	CYS	346	48.989	59.852	40.686	1.00	54.98
ATOM	2579	CA	CYS	346	49.064	58.591	39.969	1.00	55.73
ATOM	2580	C	CYS	346	48.192	57.548	40.658	1.00	56.57
ATOM	2581	O	CYS	346	48.427	57.218	41.817	1.00	58.72
ATOM	2582	CB	CYS	346	50.510	58.118	39.928	1.00	57.10
ATOM	2583	SG	CYS	346	51.587	59.170	38.905	1.00	59.00
ATOM	2584	N	LYS	347	47.174	57.042	39.966	1.00	56.79
ATOM	2585	CA	LYS	347	46.305	56.025	40.559	1.00	56.60
ATOM	2586	CB	LYS	347	44.938	55.984	39.866	1.00	56.84
ATOM	2587	CG	LYS	347	44.073	57.208	40.113	1.00	60.70
ATOM	2588	CD	LYS	347	42.609	56.931	39.810	0.01	59.47
ATOM	2589	CE	LYS	347	41.733	58.096	40.247	0.01	59.77
ATOM	2590	NZ	LYS	347	40.283	57.799	40.085	0.01	59.55
ATOM	2591	C	LYS	347	46.965	54.672	40.391	1.00	56.47
ATOM	2592	O	LYS	347	46.939	53.817	41.282	1.00	54.68
ATOM	2593	N	LYS	348	47.570	54.501	39.226	1.00	55.45
ATOM	2594	CA	LYS	348	48.219	53.261	38.873	1.00	53.89
ATOM	2595	CB	LYS	348	47.436	52.625	37.722	1.00	53.77
ATOM	2596	CG	LYS	348	47.806	51.205	37.384	1.00	57.56
ATOM	2597	CD	LYS	348	47.031	50.747	36.160	1.00	60.25
ATOM	2598	CE	LYS	348	47.394	49.329	35.769	1.00	62.70
ATOM	2599	NZ	LYS	348	46.633	48.881	34.569	1.00	66.48
ATOM	2600	C	LYS	348	49.653	53.557	38.459	1.00	52.28
ATOM	2601	O	LYS	348	49.920	54.560	37.794	1.00	53.57
ATOM	2602	N	ILE	349	50.582	52.700	38.872	1.00	49.65
ATOM	2603	CA	ILE	349	51.979	52.882	38.510	1.00	47.48
ATOM	2604	CB	ILE	349	52.854	53.153	39.732	1.00	45.57
ATOM	2605	CG2	ILE	349	54.325	52.998	39.346	1.00	46.75
ATOM	2606	CG1	ILE	349	52.575	54.561	40.259	1.00	45.22
ATOM	2607	CD1	ILE	349	53.449	54.981	41.421	1.00	43.85
ATOM	2608	C	ILE	349	52.527	51.666	37.780	1.00	46.46
ATOM	2609	O	ILE	349	52.541	50.560	38.313	1.00	45.46
ATOM	2610	N	PHE	350	52.981	51.884	36.554	1.00	45.65
ATOM	2611	CA	PHE	350	53.528	50.809	35.740	1.00	45.55
ATOM	2612	CB	PHE	350	53.276	51.106	34.259	1.00	46.63
ATOM	2613	CG	PHE	350	51.816	51.317	33.928	1.00	47.66
ATOM	2614	CD1	PHE	350	51.181	52.513	34.243	1.00	48.14
ATOM	2615	CD2	PHE	350	51.072	50.309	33.325	1.00	49.55
ATOM	2616	CE1	PHE	350	49.821	52.703	33.965	1.00	48.95
ATOM	2617	CE2	PHE	350	49.707	50.491	33.042	1.00	50.22
ATOM	2618	CZ	PHE	350	49.086	51.688	33.365	1.00	49.30
ATOM	2619	C	PHE	350	55.014	50.693	36.039	1.00	43.17

ATOM	2620	O	PHE	350	55.830	51.416	35.479	1.00	43.46
ATOM	2621	N	GLY	351	55.341	49.773	36.939	1.00	42.05
ATOM	2622	CA	GLY	351	56.712	49.578	37.370	1.00	41.42
ATOM	2623	C	GLY	351	56.740	49.343	38.875	1.00	41.84
ATOM	2624	O	GLY	351	55.744	48.905	39.452	1.00	43.39
ATOM	2625	N	SER	352	57.857	49.658	39.523	1.00	40.45
ATOM	2626	CA	SER	352	57.990	49.427	40.952	1.00	38.91
ATOM	2627	CB	SER	352	59.028	48.332	41.195	1.00	39.49
ATOM	2628	OG	SER	352	58.712	47.165	40.452	1.00	39.72
ATOM	2629	C	SER	352	58.372	50.649	41.771	1.00	39.34
ATOM	2630	O	SER	352	58.798	51.663	41.238	1.00	39.29
ATOM	2631	N	LEU	353	58.209	50.536	43.084	1.00	39.89
ATOM	2632	CA	LEU	353	58.556	51.608	44.005	1.00	39.25
ATOM	2633	CB	LEU	353	57.312	52.148	44.712	1.00	38.43
ATOM	2634	CG	LEU	353	56.288	52.925	43.887	1.00	37.43
ATOM	2635	CD1	LEU	353	55.179	53.438	44.808	1.00	35.64
ATOM	2636	CD2	LEU	353	56.980	54.089	43.190	1.00	37.71
ATOM	2637	C	LEU	353	59.504	51.030	45.032	1.00	38.86
ATOM	2638	O	LEU	353	59.224	49.994	45.633	1.00	42.35
ATOM	2639	N	ALA	354	60.636	51.685	45.227	1.00	38.83
ATOM	2640	CA	ALA	354	61.620	51.210	46.198	1.00	39.22
ATOM	2641	CB	ALA	354	62.766	50.480	45.481	1.00	34.77
ATOM	2642	C	ALA	354	62.169	52.384	47.002	1.00	39.17
ATOM	2643	O	ALA	354	62.535	53.425	46.444	1.00	39.80
ATOM	2644	N	PHE	355	62.204	52.215	48.316	1.00	39.01
ATOM	2645	CA	PHE	355	62.708	53.248	49.198	1.00	40.18
ATOM	2646	CB	PHE	355	61.615	53.702	50.177	1.00	39.58
ATOM	2647	CG	PHE	355	60.340	54.134	49.497	1.00	38.96
ATOM	2648	CD1	PHE	355	59.444	53.191	49.009	1.00	37.60
ATOM	2649	CD2	PHE	355	60.060	55.485	49.304	1.00	38.55
ATOM	2650	CE1	PHE	355	58.285	53.585	48.332	1.00	39.45
ATOM	2651	CE2	PHE	355	58.905	55.891	48.630	1.00	38.69
ATOM	2652	CZ	PHE	355	58.016	54.938	48.142	1.00	38.52
ATOM	2653	C	PHE	355	63.880	52.665	49.949	1.00	40.41
ATOM	2654	O	PHE	355	63.750	51.635	50.604	1.00	41.91
ATOM	2655	N	LEU	356	65.032	53.312	49.835	1.00	41.13
ATOM	2656	CA	LEU	356	66.230	52.838	50.513	1.00	41.92
ATOM	2657	CB	LEU	356	67.298	52.463	49.479	1.00	42.83
ATOM	2658	CG	LEU	356	67.051	51.250	48.578	1.00	45.38
ATOM	2659	CD1	LEU	356	65.821	51.477	47.695	1.00	45.56
ATOM	2660	CD2	LEU	356	68.288	51.012	47.718	1.00	46.11
ATOM	2661	C	LEU	356	66.773	53.917	51.440	1.00	41.93
ATOM	2662	O	LEU	356	66.251	55.026	51.481	1.00	40.02
ATOM	2663	N	PRO	357	67.816	53.594	52.219	1.00	44.66
ATOM	2664	CD	PRO	357	68.397	52.253	52.435	1.00	44.52
ATOM	2665	CA	PRO	357	68.409	54.571	53.134	1.00	46.97
ATOM	2666	CB	PRO	357	69.730	53.915	53.506	1.00	45.42
ATOM	2667	CG	PRO	357	69.333	52.476	53.622	1.00	45.44
ATOM	2668	C	PRO	357	68.606	55.914	52.432	1.00	50.51
ATOM	2669	O	PRO	357	68.132	56.958	52.902	1.00	51.44
ATOM	2670	N	GLU	358	69.295	55.872	51.295	1.00	52.17
ATOM	2671	CA	GLU	358	69.568	57.072	50.513	1.00	53.67
ATOM	2672	CB	GLU	358	70.243	56.688	49.194	1.00	55.12
ATOM	2673	CG	GLU	358	69.738	55.382	48.617	1.00	57.84
ATOM	2674	CD	GLU	358	70.386	55.030	47.296	1.00	58.68
ATOM	2675	OE1	GLU	358	70.171	55.782	46.315	1.00	57.40
ATOM	2676	OE2	GLU	358	71.105	54.002	47.243	1.00	57.52
ATOM	2677	C	GLU	358	68.325	57.906	50.232	1.00	53.93
ATOM	2678	O	GLU	358	68.398	59.137	50.187	1.00	53.80
ATOM	2679	N	SER	359	67.188	57.240	50.044	1.00	54.11
ATOM	2680	CA	SER	359	65.942	57.946	49.759	1.00	55.21

ATOM	2681	CB	SER	359	64.745	56.991	49.789	1.00	53.38
ATOM	2682	OG	SER	359	64.804	56.030	48.755	1.00	51.19
ATOM	2683	C	SER	359	65.707	59.049	50.776	1.00	56.90
ATOM	2684	O	SER	359	65.442	60.197	50.415	1.00	57.15
ATOM	2685	N	PHE	360	65.817	58.702	52.054	1.00	58.29
ATOM	2686	CA	PHE	360	65.583	59.682	53.102	1.00	60.53
ATOM	2687	CB	PHE	360	64.794	59.036	54.239	1.00	55.67
ATOM	2688	CG	PHE	360	63.556	58.357	53.766	1.00	52.83
ATOM	2689	CD1	PHE	360	63.555	56.991	53.499	1.00	50.96
ATOM	2690	CD2	PHE	360	62.418	59.099	53.471	1.00	51.66
ATOM	2691	CE1	PHE	360	62.441	56.378	52.942	1.00	48.89
ATOM	2692	CE2	PHE	360	61.297	58.491	52.911	1.00	49.47
ATOM	2693	CZ	PHE	360	61.311	57.130	52.646	1.00	47.46
ATOM	2694	C	PHE	360	66.851	60.347	53.607	1.00	62.88
ATOM	2695	O	PHE	360	66.785	61.388	54.259	1.00	62.93
ATOM	2696	N	ASP	361	68.002	59.751	53.300	1.00	65.54
ATOM	2697	CA	ASP	361	69.277	60.332	53.700	1.00	67.51
ATOM	2698	CB	ASP	361	70.425	59.325	53.556	1.00	66.61
ATOM	2699	CG	ASP	361	70.430	58.263	54.642	1.00	66.17
ATOM	2700	OD1	ASP	361	69.825	58.483	55.716	1.00	63.22
ATOM	2701	OD2	ASP	361	71.063	57.208	54.419	1.00	66.05
ATOM	2702	C	ASP	361	69.543	61.508	52.764	1.00	69.79
ATOM	2703	O	ASP	361	70.107	62.531	53.167	1.00	69.60
ATOM	2704	N	GLY	362	69.118	61.353	51.512	1.00	72.02
ATOM	2705	CA	GLY	362	69.335	62.388	50.518	1.00	73.73
ATOM	2706	C	GLY	362	70.783	62.338	50.073	1.00	74.63
ATOM	2707	O	GLY	362	71.641	61.849	50.805	1.00	73.91
ATOM	2708	N	ASP	363	71.064	62.819	48.869	1.00	76.81
ATOM	2709	CA	ASP	363	72.436	62.819	48.380	1.00	79.49
ATOM	2710	CB	ASP	363	72.563	61.984	47.100	1.00	80.20
ATOM	2711	CG	ASP	363	74.010	61.796	46.665	1.00	80.95
ATOM	2712	OD1	ASP	363	74.842	61.403	47.515	1.00	80.92
ATOM	2713	OD2	ASP	363	74.314	62.033	45.474	1.00	81.00
ATOM	2714	C	ASP	363	72.883	64.252	48.116	1.00	80.85
ATOM	2715	O	ASP	363	72.604	64.817	47.054	1.00	80.38
ATOM	2716	N	PRO	364	73.566	64.866	49.101	1.00	81.73
ATOM	2717	CD	PRO	364	73.770	64.322	50.458	1.00	81.93
ATOM	2718	CA	PRO	364	74.070	66.240	49.015	1.00	81.54
ATOM	2719	CB	PRO	364	74.791	66.422	50.348	1.00	81.54
ATOM	2720	CG	PRO	364	73.966	65.575	51.279	1.00	81.80
ATOM	2721	C	PRO	364	74.994	66.450	47.816	1.00	81.87
ATOM	2722	O	PRO	364	75.011	67.530	47.220	1.00	81.95
ATOM	2723	N	ALA	365	75.756	65.413	47.469	1.00	81.95
ATOM	2724	CA	ALA	365	76.676	65.471	46.334	1.00	82.33
ATOM	2725	CB	ALA	365	77.417	64.141	46.186	1.00	81.35
ATOM	2726	C	ALA	365	75.911	65.797	45.050	1.00	82.82
ATOM	2727	O	ALA	365	76.395	66.547	44.201	1.00	83.65
ATOM	2728	N	SER	366	74.715	65.233	44.913	1.00	82.50
ATOM	2729	CA	SER	366	73.885	65.484	43.740	1.00	82.52
ATOM	2730	CB	SER	366	73.148	64.206	43.329	1.00	82.26
ATOM	2731	OG	SER	366	72.287	63.753	44.360	1.00	83.81
ATOM	2732	C	SER	366	72.876	66.592	44.054	1.00	82.34
ATOM	2733	O	SER	366	72.016	66.925	43.231	1.00	81.76
ATOM	2734	N	ASN	367	73.002	67.162	45.250	1.00	82.16
ATOM	2735	CA	ASN	367	72.115	68.224	45.721	1.00	82.06
ATOM	2736	CB	ASN	367	72.221	69.465	44.830	1.00	81.56
ATOM	2737	CG	ASN	367	71.427	70.634	45.377	1.00	80.51
ATOM	2738	OD1	ASN	367	71.597	71.027	46.531	1.00	79.99
ATOM	2739	ND2	ASN	367	70.553	71.194	44.554	1.00	81.11
ATOM	2740	C	ASN	367	70.661	67.756	45.785	1.00	81.68
ATOM	2741	O	ASN	367	69.723	68.565	45.747	1.00	81.41

ATOM	2742	N	THR	368	70.486	66.439	45.872	1.00	80.67
ATOM	2743	CA	THR	368	69.167	65.832	45.979	1.00	78.44
ATOM	2744	CB	THR	368	69.172	64.390	45.435	1.00	78.87
ATOM	2745	OG1	THR	368	70.291	63.679	45.982	1.00	78.61
ATOM	2746	CG2	THR	368	69.270	64.395	43.913	1.00	78.71
ATOM	2747	C	THR	368	68.846	65.822	47.470	1.00	77.12
ATOM	2748	O	THR	368	69.304	64.953	48.214	1.00	76.03
ATOM	2749	N	ALA	369	68.077	66.816	47.901	1.00	76.38
ATOM	2750	CA	ALA	369	67.709	66.944	49.300	1.00	76.74
ATOM	2751	CB	ALA	369	66.828	68.169	49.498	1.00	76.05
ATOM	2752	C	ALA	369	66.984	65.696	49.782	1.00	77.16
ATOM	2753	O	ALA	369	66.275	65.042	49.016	1.00	78.07
ATOM	2754	N	PRO	370	67.173	65.332	51.059	1.00	76.47
ATOM	2755	CD	PRO	370	68.080	65.903	52.075	1.00	75.55
ATOM	2756	CA	PRO	370	66.492	64.143	51.570	1.00	74.73
ATOM	2757	CB	PRO	370	66.781	64.208	53.063	1.00	75.53
ATOM	2758	CG	PRO	370	68.175	64.779	53.089	1.00	75.54
ATOM	2759	C	PRO	370	65.003	64.232	51.258	1.00	73.48
ATOM	2760	O	PRO	370	64.473	65.313	50.992	1.00	72.25
ATOM	2761	N	LEU	371	64.331	63.092	51.267	1.00	72.66
ATOM	2762	CA	LEU	371	62.909	63.078	50.987	1.00	70.92
ATOM	2763	CB	LEU	371	62.488	61.699	50.484	1.00	70.30
ATOM	2764	CG	LEU	371	61.186	61.639	49.689	1.00	70.82
ATOM	2765	CD1	LEU	371	61.188	62.676	48.576	1.00	70.62
ATOM	2766	CD2	LEU	371	61.034	60.249	49.110	1.00	71.78
ATOM	2767	C	LEU	371	62.231	63.419	52.304	1.00	70.26
ATOM	2768	O	LEU	371	62.697	63.006	53.367	1.00	70.33
ATOM	2769	N	GLN	372	61.153	64.193	52.236	1.00	69.31
ATOM	2770	CA	GLN	372	60.439	64.604	53.437	1.00	68.71
ATOM	2771	CB	GLN	372	60.097	66.098	53.371	1.00	69.99
ATOM	2772	CG	GLN	372	61.321	66.998	53.286	1.00	71.40
ATOM	2773	CD	GLN	372	62.246	66.847	54.484	1.00	71.80
ATOM	2774	OE1	GLN	372	63.432	67.164	54.405	1.00	71.93
ATOM	2775	NE2	GLN	372	61.703	66.368	55.601	1.00	71.67
ATOM	2776	C	GLN	372	59.170	63.805	53.646	1.00	67.36
ATOM	2777	O	GLN	372	58.424	63.546	52.703	1.00	67.20
ATOM	2778	N	PRO	373	58.907	63.408	54.897	1.00	65.94
ATOM	2779	CD	PRO	373	59.725	63.676	56.094	1.00	64.60
ATOM	2780	CA	PRO	373	57.716	62.631	55.241	1.00	66.02
ATOM	2781	CB	PRO	373	57.665	62.753	56.759	1.00	65.24
ATOM	2782	CG	PRO	373	59.117	62.742	57.119	1.00	64.73
ATOM	2783	C	PRO	373	56.442	63.140	54.565	1.00	66.69
ATOM	2784	O	PRO	373	55.578	62.349	54.191	1.00	66.11
ATOM	2785	N	GLU	374	56.336	64.458	54.402	1.00	67.78
ATOM	2786	CA	GLU	374	55.155	65.063	53.783	1.00	67.96
ATOM	2787	CB	GLU	374	55.102	66.571	54.062	1.00	71.04
ATOM	2788	CG	GLU	374	55.353	66.977	55.511	1.00	76.32
ATOM	2789	CD	GLU	374	56.834	67.069	55.836	1.00	79.67
ATOM	2790	OE1	GLU	374	57.560	67.749	55.073	1.00	82.11
ATOM	2791	OE2	GLU	374	57.269	66.474	56.851	1.00	80.79
ATOM	2792	C	GLU	374	55.130	64.839	52.276	1.00	65.88
ATOM	2793	O	GLU	374	54.068	64.852	51.652	1.00	64.80
ATOM	2794	N	GLN	375	56.306	64.650	51.690	1.00	64.56
ATOM	2795	CA	GLN	375	56.406	64.422	50.255	1.00	63.02
ATOM	2796	CB	GLN	375	57.873	64.533	49.816	1.00	63.52
ATOM	2797	CG	GLN	375	58.463	65.934	50.022	1.00	64.59
ATOM	2798	CD	GLN	375	59.898	66.082	49.511	1.00	65.39
ATOM	2799	OE1	GLN	375	60.853	65.602	50.131	1.00	64.63
ATOM	2800	NE2	GLN	375	60.048	66.750	48.370	1.00	64.25
ATOM	2801	C	GLN	375	55.819	63.048	49.894	1.00	61.79
ATOM	2802	O	GLN	375	55.289	62.852	48.796	1.00	59.93

ATOM	2803	N	LEU	376	55.893	62.111	50.836	1.00	60.12
ATOM	2804	CA	LEU	376	55.370	60.767	50.628	1.00	58.67
ATOM	2805	CB	LEU	376	55.747	59.865	51.807	1.00	56.26
ATOM	2806	CG	LEU	376	57.233	59.609	52.064	1.00	54.81
ATOM	2807	CD1	LEU	376	57.400	58.770	53.323	1.00	52.63
ATOM	2808	CD2	LEU	376	57.847	58.909	50.870	1.00	52.72
ATOM	2809	C	LEU	376	53.848	60.757	50.452	1.00	58.95
ATOM	2810	O	LEU	376	53.275	59.771	49.996	1.00	57.95
ATOM	2811	N	GLN	377	53.195	61.855	50.812	1.00	60.33
ATOM	2812	CA	GLN	377	51.740	61.936	50.694	1.00	62.04
ATOM	2813	CB	GLN	377	51.225	63.212	51.374	1.00	64.78
ATOM	2814	CG	GLN	377	51.792	63.448	52.782	1.00	69.22
ATOM	2815	CD	GLN	377	51.407	62.363	53.783	1.00	72.43
ATOM	2816	OE1	GLN	377	51.981	62.273	54.881	1.00	73.12
ATOM	2817	NE2	GLN	377	50.426	61.541	53.415	1.00	72.94
ATOM	2818	C	GLN	377	51.332	61.910	49.221	1.00	60.41
ATOM	2819	O	GLN	377	50.155	62.000	48.879	1.00	59.09
ATOM	2820	N	VAL	378	52.324	61.784	48.353	1.00	59.46
ATOM	2821	CA	VAL	378	52.086	61.732	46.922	1.00	59.66
ATOM	2822	CB	VAL	378	53.421	61.887	46.152	1.00	59.85
ATOM	2823	CG1	VAL	378	53.229	61.598	44.679	1.00	61.73
ATOM	2824	CG2	VAL	378	53.948	63.297	46.326	1.00	61.51
ATOM	2825	C	VAL	378	51.411	60.416	46.511	1.00	59.34
ATOM	2826	O	VAL	378	50.664	60.369	45.531	1.00	59.84
ATOM	2827	N	PHE	379	51.651	59.353	47.268	1.00	57.35
ATOM	2828	CA	PHE	379	51.077	58.060	46.922	1.00	57.45
ATOM	2829	CB	PHE	379	52.025	56.942	47.348	1.00	54.33
ATOM	2830	CG	PHE	379	53.397	57.072	46.773	1.00	51.15
ATOM	2831	CD1	PHE	379	54.446	57.542	47.547	1.00	49.57
ATOM	2832	CD2	PHE	379	53.635	56.758	45.445	1.00	49.60
ATOM	2833	CE1	PHE	379	55.716	57.700	47.009	1.00	47.98
ATOM	2834	CE2	PHE	379	54.906	56.914	44.899	1.00	49.85
ATOM	2835	CZ	PHE	379	55.946	57.386	45.687	1.00	46.39
ATOM	2836	C	PHE	379	49.699	57.779	47.491	1.00	59.16
ATOM	2837	O	PHE	379	49.169	56.675	47.323	1.00	59.83
ATOM	2838	N	GLU	380	49.107	58.773	48.141	1.00	60.36
ATOM	2839	CA	GLU	380	47.800	58.580	48.750	1.00	60.34
ATOM	2840	CB	GLU	380	47.431	59.804	49.595	1.00	64.04
ATOM	2841	CG	GLU	380	48.559	60.216	50.561	1.00	69.08
ATOM	2842	CD	GLU	380	48.062	60.875	51.841	1.00	71.31
ATOM	2843	OE1	GLU	380	47.450	60.167	52.670	1.00	72.79
ATOM	2844	OE2	GLU	380	48.286	62.096	52.018	1.00	73.08
ATOM	2845	C	GLU	380	46.705	58.257	47.746	1.00	58.30
ATOM	2846	O	GLU	380	45.672	57.700	48.110	1.00	58.43
ATOM	2847	N	THR	381	46.927	58.583	46.479	1.00	55.99
ATOM	2848	CA	THR	381	45.924	58.284	45.461	1.00	55.42
ATOM	2849	CB	THR	381	45.879	59.387	44.369	1.00	57.10
ATOM	2850	OG1	THR	381	47.178	59.545	43.787	1.00	58.07
ATOM	2851	CG2	THR	381	45.442	60.718	44.967	1.00	55.87
ATOM	2852	C	THR	381	46.219	56.936	44.798	1.00	54.20
ATOM	2853	O	THR	381	45.359	56.357	44.125	1.00	53.97
ATOM	2854	N	LEU	382	47.440	56.442	45.013	1.00	52.85
ATOM	2855	CA	LEU	382	47.907	55.179	44.444	1.00	49.26
ATOM	2856	CB	LEU	382	49.377	54.959	44.820	1.00	47.79
ATOM	2857	CG	LEU	382	50.073	53.734	44.210	1.00	46.53
ATOM	2858	CD1	LEU	382	50.071	53.838	42.693	1.00	42.81
ATOM	2859	CD2	LEU	382	51.493	53.635	44.736	1.00	46.51
ATOM	2860	C	LEU	382	47.078	53.956	44.850	1.00	48.27
ATOM	2861	O	LEU	382	46.925	53.656	46.031	1.00	47.89
ATOM	2862	N	GLU	383	46.564	53.252	43.848	1.00	46.86
ATOM	2863	CA	GLU	383	45.742	52.067	44.047	1.00	48.66

ATOM	2864	CB	GLU	383	44.392	52.251	43.340	1.00	49.79
ATOM	2865	CG	GLU	383	43.444	53.219	44.030	1.00	54.40
ATOM	2866	CD	GLU	383	42.353	53.762	43.110	1.00	54.51
ATOM	2867	OE1	GLU	383	41.654	52.965	42.440	1.00	52.52
ATOM	2868	OE2	GLU	383	42.194	55.002	43.071	1.00	57.33
ATOM	2869	C	GLU	383	46.398	50.792	43.511	1.00	48.27
ATOM	2870	O	GLU	383	46.054	49.681	43.941	1.00	48.13
ATOM	2871	N	GLU	384	47.338	50.956	42.579	1.00	46.27
ATOM	2872	CA	GLU	384	47.998	49.818	41.948	1.00	43.47
ATOM	2873	CB	GLU	384	47.182	49.377	40.727	1.00	43.66
ATOM	2874	CG	GLU	384	47.716	48.150	39.991	1.00	44.19
ATOM	2875	CD	GLU	384	46.854	47.776	38.783	1.00	46.00
ATOM	2876	OE1	GLU	384	45.688	48.226	38.712	1.00	49.83
ATOM	2877	OE2	GLU	384	47.331	47.027	37.908	1.00	45.41
ATOM	2878	C	GLU	384	49.444	50.030	41.510	1.00	41.83
ATOM	2879	O	GLU	384	49.822	51.096	41.028	1.00	38.67
ATOM	2880	N	ILE	385	50.232	48.973	41.684	1.00	40.65
ATOM	2881	CA	ILE	385	51.636	48.925	41.301	1.00	37.49
ATOM	2882	CB	ILE	385	52.569	48.874	42.535	1.00	36.30
ATOM	2883	CG2	ILE	385	53.981	48.449	42.110	1.00	35.11
ATOM	2884	CG1	ILE	385	52.581	50.238	43.239	1.00	35.95
ATOM	2885	CD1	ILE	385	53.340	50.264	44.568	1.00	29.52
ATOM	2886	C	ILE	385	51.766	47.616	40.532	1.00	36.95
ATOM	2887	O	ILE	385	51.464	46.556	41.068	1.00	35.48
ATOM	2888	N	THR	386	52.196	47.684	39.277	1.00	37.82
ATOM	2889	CA	THR	386	52.341	46.475	38.474	1.00	37.30
ATOM	2890	CB	THR	386	52.386	46.786	36.949	1.00	39.40
ATOM	2891	OG1	THR	386	53.414	47.751	36.670	1.00	37.23
ATOM	2892	CG2	THR	386	51.027	47.308	36.477	1.00	38.44
ATOM	2893	C	THR	386	53.615	45.746	38.861	1.00	38.20
ATOM	2894	O	THR	386	53.722	44.521	38.684	1.00	38.03
ATOM	2895	N	GLY	387	54.574	46.497	39.398	1.00	36.02
ATOM	2896	CA	GLY	387	55.834	45.896	39.805	1.00	36.07
ATOM	2897	C	GLY	387	55.839	45.377	41.231	1.00	35.54
ATOM	2898	O	GLY	387	55.028	44.527	41.601	1.00	37.73
ATOM	2899	N	TYR	388	56.759	45.877	42.041	1.00	33.72
ATOM	2900	CA	TYR	388	56.845	45.438	43.426	1.00	34.18
ATOM	2901	CB	TYR	388	58.033	44.481	43.603	1.00	33.76
ATOM	2902	CG	TYR	388	59.384	45.087	43.268	1.00	33.25
ATOM	2903	CD1	TYR	388	60.077	45.871	44.198	1.00	35.21
ATOM	2904	CE1	TYR	388	61.317	46.446	43.886	1.00	33.69
ATOM	2905	CD2	TYR	388	59.963	44.895	42.013	1.00	33.97
ATOM	2906	CE2	TYR	388	61.199	45.470	41.685	1.00	33.20
ATOM	2907	CZ	TYR	388	61.870	46.238	42.626	1.00	34.87
ATOM	2908	OH	TYR	388	63.097	46.782	42.308	1.00	34.96
ATOM	2909	C	TYR	388	57.013	46.651	44.322	1.00	34.08
ATOM	2910	O	TYR	388	57.157	47.776	43.842	1.00	36.49
ATOM	2911	N	LEU	389	56.967	46.432	45.624	1.00	32.82
ATOM	2912	CA	LEU	389	57.163	47.522	46.559	1.00	33.35
ATOM	2913	CB	LEU	389	55.872	47.816	47.334	1.00	33.62
ATOM	2914	CG	LEU	389	55.963	48.815	48.497	1.00	34.53
ATOM	2915	CD1	LEU	389	56.529	50.133	47.997	1.00	34.74
ATOM	2916	CD2	LEU	389	54.583	49.036	49.132	1.00	33.40
ATOM	2917	C	LEU	389	58.269	47.031	47.480	1.00	34.94
ATOM	2918	O	LEU	389	58.185	45.934	48.050	1.00	34.97
ATOM	2919	N	TYR	390	59.322	47.832	47.594	1.00	35.52
ATOM	2920	CA	TYR	390	60.472	47.490	48.426	1.00	36.11
ATOM	2921	CB	TYR	390	61.687	47.241	47.515	1.00	36.83
ATOM	2922	CG	TYR	390	62.984	46.903	48.215	1.00	36.84
ATOM	2923	CD1	TYR	390	63.449	45.588	48.260	1.00	39.20
ATOM	2924	CE1	TYR	390	64.675	45.269	48.865	1.00	39.01

ATOM	2925	CD2	TYR	390	63.770	47.902	48.800	1.00	36.30
ATOM	2926	CE2	TYR	390	64.997	47.594	49.415	1.00	37.61
ATOM	2927	CZ	TYR	390	65.441	46.278	49.440	1.00	38.56
ATOM	2928	OH	TYR	390	66.642	45.965	50.034	1.00	40.00
ATOM	2929	C	TYR	390	60.722	48.675	49.359	1.00	36.57
ATOM	2930	O	TYR	390	60.818	49.812	48.902	1.00	39.11
ATOM	2931	N	ILE	391	60.826	48.411	50.656	1.00	34.84
ATOM	2932	CA	ILE	391	61.047	49.461	51.634	1.00	36.11
ATOM	2933	CB	ILE	391	59.742	49.799	52.392	1.00	38.59
ATOM	2934	CG2	ILE	391	59.975	50.992	53.304	1.00	33.31
ATOM	2935	CG1	ILE	391	58.606	50.080	51.394	1.00	37.52
ATOM	2936	CD1	ILE	391	57.306	50.498	52.045	1.00	36.81
ATOM	2937	C	ILE	391	62.082	49.024	52.657	1.00	37.80
ATOM	2938	O	ILE	391	61.784	48.240	53.558	1.00	39.48
ATOM	2939	N	SER	392	63.296	49.541	52.524	1.00	38.87
ATOM	2940	CA	SER	392	64.376	49.186	53.438	1.00	39.77
ATOM	2941	CB	SER	392	65.609	48.743	52.652	1.00	40.15
ATOM	2942	OG	SER	392	66.009	49.756	51.739	1.00	42.76
ATOM	2943	C	SER	392	64.722	50.370	54.320	1.00	38.92
ATOM	2944	O	SER	392	65.679	50.325	55.090	1.00	38.90
ATOM	2945	N	ALA	393	63.941	51.435	54.185	1.00	38.10
ATOM	2946	CA	ALA	393	64.117	52.637	54.987	1.00	39.21
ATOM	2947	CB	ALA	393	65.262	53.492	54.444	1.00	38.87
ATOM	2948	C	ALA	393	62.809	53.424	54.978	1.00	40.68
ATOM	2949	O	ALA	393	62.103	53.488	53.963	1.00	38.40
ATOM	2950	N	TRP	394	62.488	54.019	56.120	1.00	41.96
ATOM	2951	CA	TRP	394	61.252	54.775	56.264	1.00	43.86
ATOM	2952	CB	TRP	394	60.110	53.794	56.583	1.00	42.73
ATOM	2953	CG	TRP	394	58.729	54.325	56.387	1.00	42.06
ATOM	2954	CD2	TRP	394	58.072	54.578	55.139	1.00	41.48
ATOM	2955	CE2	TRP	394	56.780	55.068	55.438	1.00	40.33
ATOM	2956	CE3	TRP	394	58.448	54.439	53.797	1.00	41.31
ATOM	2957	CD1	TRP	394	57.839	54.661	57.361	1.00	43.59
ATOM	2958	NE1	TRP	394	56.664	55.107	56.801	1.00	43.49
ATOM	2959	CZ2	TRP	394	55.862	55.421	54.447	1.00	39.55
ATOM	2960	CZ3	TRP	394	57.528	54.793	52.803	1.00	41.64
ATOM	2961	CH2	TRP	394	56.249	55.278	53.140	1.00	40.34
ATOM	2962	C	TRP	394	61.508	55.748	57.415	1.00	44.64
ATOM	2963	O	TRP	394	62.259	55.427	58.335	1.00	42.87
ATOM	2964	N	PRO	395	60.907	56.954	57.366	1.00	46.80
ATOM	2965	CD	PRO	395	59.942	57.432	56.356	1.00	47.29
ATOM	2966	CA	PRO	395	61.096	57.963	58.420	1.00	48.66
ATOM	2967	CB	PRO	395	60.358	59.184	57.859	1.00	48.97
ATOM	2968	CG	PRO	395	59.242	58.576	57.079	1.00	47.43
ATOM	2969	C	PRO	395	60.565	57.543	59.785	1.00	49.74
ATOM	2970	O	PRO	395	59.376	57.256	59.917	1.00	50.66
ATOM	2971	N	ASP	396	61.438	57.512	60.795	1.00	51.99
ATOM	2972	CA	ASP	396	61.033	57.121	62.153	1.00	54.46
ATOM	2973	CB	ASP	396	62.155	57.360	63.164	1.00	56.07
ATOM	2974	CG	ASP	396	63.283	56.373	63.022	1.00	61.08
ATOM	2975	OD1	ASP	396	62.993	55.169	62.829	1.00	62.53
ATOM	2976	OD2	ASP	396	64.458	56.799	63.115	1.00	63.88
ATOM	2977	C	ASP	396	59.790	57.850	62.645	1.00	54.39
ATOM	2978	O	ASP	396	58.986	57.289	63.390	1.00	54.40
ATOM	2979	N	SER	397	59.635	59.103	62.238	1.00	53.50
ATOM	2980	CA	SER	397	58.475	59.870	62.653	1.00	54.04
ATOM	2981	CB	SER	397	58.551	61.287	62.085	1.00	53.63
ATOM	2982	OG	SER	397	58.623	61.262	60.673	1.00	56.20
ATOM	2983	C	SER	397	57.161	59.199	62.229	1.00	53.65
ATOM	2984	O	SER	397	56.164	59.288	62.951	1.00	56.24
ATOM	2985	N	LEU	398	57.150	58.532	61.074	1.00	50.45

ATOM	2986	CA	LEU	398	55.936	57.858	60.606	1.00	49.41
ATOM	2987	CB	LEU	398	55.917	57.766	59.075	1.00	47.89
ATOM	2988	CG	LEU	398	55.848	59.089	58.296	1.00	48.30
ATOM	2989	CD1	LEU	398	55.639	58.783	56.834	1.00	47.77
ATOM	2990	CD2	LEU	398	54.706	59.967	58.798	1.00	46.68
ATOM	2991	C	LEU	398	55.801	56.457	61.220	1.00	47.95
ATOM	2992	O	LEU	398	56.700	55.627	61.100	1.00	47.18
ATOM	2993	N	PRO	399	54.662	56.182	61.885	1.00	45.97
ATOM	2994	CD	PRO	399	53.594	57.154	62.195	1.00	42.77
ATOM	2995	CA	PRO	399	54.393	54.892	62.533	1.00	45.25
ATOM	2996	CB	PRO	399	53.327	55.254	63.566	1.00	44.03
ATOM	2997	CG	PRO	399	52.528	56.285	62.842	1.00	43.17
ATOM	2998	C	PRO	399	53.940	53.753	61.618	1.00	45.16
ATOM	2999	O	PRO	399	54.021	52.575	61.991	1.00	46.16
ATOM	3000	N	ASP	400	53.451	54.093	60.434	1.00	42.35
ATOM	3001	CA	ASP	400	52.987	53.069	59.512	1.00	41.88
ATOM	3002	CB	ASP	400	51.493	52.790	59.736	1.00	42.58
ATOM	3003	CG	ASP	400	50.617	54.024	59.516	1.00	44.56
ATOM	3004	OD1	ASP	400	51.096	55.030	58.943	1.00	44.51
ATOM	3005	OD2	ASP	400	49.434	53.983	59.912	1.00	45.18
ATOM	3006	C	ASP	400	53.229	53.461	58.062	1.00	41.12
ATOM	3007	O	ASP	400	53.945	54.425	57.779	1.00	41.52
ATOM	3008	N	LEU	401	52.630	52.711	57.144	1.00	39.96
ATOM	3009	CA	LEU	401	52.787	52.985	55.718	1.00	40.52
ATOM	3010	CB	LEU	401	53.207	51.704	54.986	1.00	37.20
ATOM	3011	CG	LEU	401	54.389	50.918	55.572	1.00	34.86
ATOM	3012	CD1	LEU	401	54.417	49.516	54.978	1.00	29.03
ATOM	3013	CD2	LEU	401	55.697	51.668	55.317	1.00	32.51
ATOM	3014	C	LEU	401	51.445	53.481	55.178	1.00	42.33
ATOM	3015	O	LEU	401	51.102	53.249	54.010	1.00	42.00
ATOM	3016	N	SER	402	50.691	54.174	56.029	1.00	43.15
ATOM	3017	CA	SER	402	49.376	54.659	55.635	1.00	45.17
ATOM	3018	CB	SER	402	48.704	55.422	56.790	1.00	46.37
ATOM	3019	OG	SER	402	49.390	56.621	57.108	1.00	50.42
ATOM	3020	C	SER	402	49.379	55.505	54.360	1.00	45.55
ATOM	3021	O	SER	402	48.332	55.649	53.718	1.00	44.73
ATOM	3022	N	VAL	403	50.531	56.059	53.977	1.00	43.17
ATOM	3023	CA	VAL	403	50.562	56.833	52.746	1.00	44.06
ATOM	3024	CB	VAL	403	51.995	57.324	52.361	1.00	46.39
ATOM	3025	CG1	VAL	403	52.570	58.199	53.450	1.00	45.24
ATOM	3026	CG2	VAL	403	52.908	56.131	52.075	1.00	48.94
ATOM	3027	C	VAL	403	50.056	55.922	51.625	1.00	43.40
ATOM	3028	O	VAL	403	49.513	56.397	50.624	1.00	44.33
ATOM	3029	N	PHE	404	50.238	54.614	51.797	1.00	40.95
ATOM	3030	CA	PHE	404	49.795	53.636	50.804	1.00	41.83
ATOM	3031	CB	PHE	404	50.849	52.528	50.636	1.00	42.48
ATOM	3032	CG	PHE	404	52.148	53.000	50.065	1.00	39.30
ATOM	3033	CD1	PHE	404	52.217	53.489	48.770	1.00	38.75
ATOM	3034	CD2	PHE	404	53.306	52.953	50.825	1.00	38.89
ATOM	3035	CE1	PHE	404	53.426	53.921	48.245	1.00	38.45
ATOM	3036	CE2	PHE	404	54.519	53.383	50.307	1.00	37.33
ATOM	3037	CZ	PHE	404	54.577	53.866	49.017	1.00	37.18
ATOM	3038	C	PHE	404	48.472	52.990	51.220	1.00	42.45
ATOM	3039	O	PHE	404	48.150	51.877	50.792	1.00	39.55
ATOM	3040	N	GLN	405	47.699	53.687	52.045	1.00	44.33
ATOM	3041	CA	GLN	405	46.442	53.130	52.520	1.00	45.10
ATOM	3042	CB	GLN	405	45.816	54.054	53.564	1.00	45.82
ATOM	3043	CG	GLN	405	45.431	55.426	53.053	1.00	51.73
ATOM	3044	CD	GLN	405	44.871	56.304	54.156	1.00	53.97
ATOM	3045	OE1	GLN	405	43.860	55.960	54.778	1.00	54.78
ATOM	3046	NE2	GLN	405	45.527	57.443	54.411	1.00	53.84

ATOM	3047	C	GLN	405	45.426	52.790	51.429	1.00	44.71
ATOM	3048	O	GLN	405	44.518	51.996	51.667	1.00	45.50
ATOM	3049	N	ASN	406	45.565	53.368	50.239	1.00	43.57
ATOM	3050	CA	ASN	406	44.624	53.056	49.160	1.00	44.72
ATOM	3051	CB	ASN	406	44.169	54.326	48.421	1.00	46.41
ATOM	3052	CG	ASN	406	43.366	55.270	49.299	1.00	47.55
ATOM	3053	OD1	ASN	406	42.443	54.858	50.011	1.00	45.86
ATOM	3054	ND2	ASN	406	43.705	56.555	49.236	1.00	46.55
ATOM	3055	C	ASN	406	45.223	52.094	48.137	1.00	44.32
ATOM	3056	O	ASN	406	44.677	51.917	47.044	1.00	45.85
ATOM	3057	N	LEU	407	46.355	51.492	48.482	1.00	42.87
ATOM	3058	CA	LEU	407	47.011	50.546	47.595	1.00	41.65
ATOM	3059	CB	LEU	407	48.438	50.296	48.078	1.00	39.43
ATOM	3060	CG	LEU	407	49.305	49.362	47.244	1.00	38.68
ATOM	3061	CD1	LEU	407	49.279	49.793	45.796	1.00	37.29
ATOM	3062	CD2	LEU	407	50.718	49.377	47.794	1.00	39.44
ATOM	3063	C	LEU	407	46.191	49.257	47.627	1.00	42.87
ATOM	3064	O	LEU	407	46.066	48.618	48.668	1.00	41.20
ATOM	3065	N	GLN	408	45.626	48.880	46.487	1.00	44.64
ATOM	3066	CA	GLN	408	44.789	47.686	46.422	1.00	46.93
ATOM	3067	CB	GLN	408	43.540	47.979	45.599	1.00	46.58
ATOM	3068	CG	GLN	408	42.557	48.874	46.317	1.00	51.50
ATOM	3069	CD	GLN	408	41.587	49.554	45.374	1.00	52.88
ATOM	3070	OE1	GLN	408	40.933	48.907	44.545	1.00	52.20
ATOM	3071	NE2	GLN	408	41.486	50.872	45.497	1.00	55.91
ATOM	3072	C	GLN	408	45.464	46.458	45.852	1.00	47.02
ATOM	3073	O	GLN	408	45.213	45.334	46.300	1.00	47.65
ATOM	3074	N	VAL	409	46.317	46.672	44.861	1.00	44.93
ATOM	3075	CA	VAL	409	46.984	45.562	44.227	1.00	44.05
ATOM	3076	CB	VAL	409	46.259	45.169	42.920	1.00	45.18
ATOM	3077	CG1	VAL	409	47.031	44.075	42.194	1.00	45.20
ATOM	3078	CG2	VAL	409	44.850	44.698	43.231	1.00	47.18
ATOM	3079	C	VAL	409	48.434	45.835	43.890	1.00	43.61
ATOM	3080	O	VAL	409	48.813	46.949	43.528	1.00	42.67
ATOM	3081	N	ILE	410	49.239	44.791	44.038	1.00	41.59
ATOM	3082	CA	ILE	410	50.644	44.823	43.693	1.00	38.73
ATOM	3083	CB	ILE	410	51.557	44.752	44.937	1.00	34.96
ATOM	3084	CG2	ILE	410	53.034	44.643	44.501	1.00	30.70
ATOM	3085	CG1	ILE	410	51.347	46.003	45.793	1.00	30.25
ATOM	3086	CD1	ILE	410	52.241	46.107	47.012	1.00	25.93
ATOM	3087	C	ILE	410	50.752	43.546	42.877	1.00	39.73
ATOM	3088	O	ILE	410	50.887	42.461	43.435	1.00	40.26
ATOM	3089	N	ARG	411	50.630	43.680	41.556	1.00	41.18
ATOM	3090	CA	ARG	411	50.694	42.536	40.651	1.00	41.50
ATOM	3091	CB	ARG	411	50.614	42.987	39.193	1.00	44.32
ATOM	3092	CG	ARG	411	49.216	43.133	38.611	1.00	50.54
ATOM	3093	CD	ARG	411	48.556	44.418	39.037	1.00	54.13
ATOM	3094	NE	ARG	411	47.302	44.679	38.322	1.00	60.27
ATOM	3095	CZ	ARG	411	46.201	43.930	38.392	1.00	61.55
ATOM	3096	NH1	ARG	411	46.162	42.836	39.144	1.00	59.64
ATOM	3097	NH2	ARG	411	45.118	44.299	37.719	1.00	63.09
ATOM	3098	C	ARG	411	51.961	41.720	40.819	1.00	41.76
ATOM	3099	O	ARG	411	51.927	40.494	40.760	1.00	43.44
ATOM	3100	N	GLY	412	53.086	42.392	41.018	1.00	40.54
ATOM	3101	CA	GLY	412	54.327	41.659	41.154	1.00	41.36
ATOM	3102	C	GLY	412	54.784	41.094	39.815	1.00	41.71
ATOM	3103	O	GLY	412	55.437	40.055	39.771	1.00	39.26
ATOM	3104	N	ARG	413	54.436	41.770	38.717	1.00	43.65
ATOM	3105	CA	ARG	413	54.857	41.316	37.391	1.00	44.63
ATOM	3106	CB	ARG	413	54.234	42.165	36.287	1.00	45.78
ATOM	3107	CG	ARG	413	52.743	41.912	36.102	1.00	49.28

ATOM	3108	CD	ARG	413	52.314	42.174	34.661	1.00	50.29
ATOM	3109	NE	ARG	413	51.307	43.227	34.552	1.00	53.86
ATOM	3110	CZ	ARG	413	50.043	43.113	34.950	1.00	51.79
ATOM	3111	NH1	ARG	413	49.608	41.978	35.493	1.00	50.37
ATOM	3112	NH2	ARG	413	49.217	44.142	34.799	1.00	48.50
ATOM	3113	C	ARG	413	56.373	41.398	37.331	1.00	44.29
ATOM	3114	O	ARG	413	57.008	40.727	36.524	1.00	46.07
ATOM	3115	N	ILE	414	56.938	42.242	38.186	1.00	42.36
ATOM	3116	CA	ILE	414	58.380	42.380	38.311	1.00	41.85
ATOM	3117	CB	ILE	414	58.868	43.768	37.862	1.00	41.95
ATOM	3118	CG2	ILE	414	60.374	43.869	38.024	1.00	38.29
ATOM	3119	CG1	ILE	414	58.504	44.006	36.401	1.00	42.75
ATOM	3120	CD1	ILE	414	58.947	45.376	35.886	1.00	45.50
ATOM	3121	C	ILE	414	58.632	42.209	39.820	1.00	42.04
ATOM	3122	O	ILE	414	58.010	42.896	40.634	1.00	42.22
ATOM	3123	N	LEU	415	59.525	41.293	40.194	1.00	40.03
ATOM	3124	CA	LEU	415	59.807	41.040	41.608	1.00	39.68
ATOM	3125	CB	LEU	415	59.630	39.553	41.915	1.00	37.15
ATOM	3126	CG	LEU	415	58.331	38.933	41.382	1.00	37.95
ATOM	3127	CD1	LEU	415	58.434	37.428	41.472	1.00	34.92
ATOM	3128	CD2	LEU	415	57.118	39.454	42.150	1.00	36.11
ATOM	3129	C	LEU	415	61.202	41.475	42.029	1.00	38.94
ATOM	3130	O	LEU	415	62.129	41.464	41.229	1.00	40.10
ATOM	3131	N	HIS	416	61.351	41.870	43.286	1.00	37.91
ATOM	3132	CA	HIS	416	62.661	42.277	43.765	1.00	37.95
ATOM	3133	CB	HIS	416	62.549	42.958	45.117	1.00	35.21
ATOM	3134	CG	HIS	416	63.853	43.482	45.611	1.00	37.67
ATOM	3135	CD2	HIS	416	64.475	44.666	45.396	1.00	36.84
ATOM	3136	ND1	HIS	416	64.735	42.708	46.333	1.00	37.22
ATOM	3137	CE1	HIS	416	65.846	43.394	46.540	1.00	38.59
ATOM	3138	NE2	HIS	416	65.714	44.584	45.981	1.00	36.63
ATOM	3139	C	HIS	416	63.520	41.011	43.849	1.00	38.20
ATOM	3140	O	HIS	416	63.062	39.973	44.355	1.00	37.39
ATOM	3141	N	ASN	417	64.760	41.092	43.359	1.00	36.97
ATOM	3142	CA	ASN	417	65.634	39.913	43.298	1.00	35.90
ATOM	3143	CB	ASN	417	66.035	39.399	44.683	1.00	38.02
ATOM	3144	CG	ASN	417	67.226	40.139	45.260	1.00	40.21
ATOM	3145	OD1	ASN	417	68.074	40.625	44.525	1.00	44.23
ATOM	3146	ND2	ASN	417	67.304	40.210	46.582	1.00	39.54
ATOM	3147	C	ASN	417	64.845	38.823	42.562	1.00	36.30
ATOM	3148	O	ASN	417	65.093	37.631	42.738	1.00	35.72
ATOM	3149	N	GLY	418	63.883	39.252	41.747	1.00	33.78
ATOM	3150	CA	GLY	418	63.071	38.327	40.989	1.00	34.34
ATOM	3151	C	GLY	418	62.245	37.374	41.831	1.00	35.85
ATOM	3152	O	GLY	418	61.760	36.363	41.323	1.00	37.04
ATOM	3153	N	ALA	419	62.055	37.690	43.108	1.00	35.17
ATOM	3154	CA	ALA	419	61.296	36.793	43.972	1.00	34.41
ATOM	3155	CB	ALA	419	62.275	35.987	44.854	1.00	30.62
ATOM	3156	C	ALA	419	60.226	37.444	44.855	1.00	33.91
ATOM	3157	O	ALA	419	59.134	36.893	45.021	1.00	33.84
ATOM	3158	N	TYR	420	60.547	38.611	45.405	1.00	33.11
ATOM	3159	CA	TYR	420	59.672	39.325	46.327	1.00	31.95
ATOM	3160	CB	TYR	420	60.514	39.806	47.505	1.00	33.26
ATOM	3161	CG	TYR	420	61.335	38.713	48.139	1.00	34.39
ATOM	3162	CD1	TYR	420	62.715	38.640	47.936	1.00	37.18
ATOM	3163	CE1	TYR	420	63.487	37.626	48.541	1.00	38.42
ATOM	3164	CD2	TYR	420	60.733	37.749	48.958	1.00	35.52
ATOM	3165	CE2	TYR	420	61.486	36.738	49.562	1.00	37.85
ATOM	3166	CZ	TYR	420	62.862	36.681	49.351	1.00	38.60
ATOM	3167	OH	TYR	420	63.595	35.676	49.942	1.00	39.21
ATOM	3168	C	TYR	420	58.879	40.497	45.764	1.00	31.18

ATOM	3169	O	TYR	420	59.442	41.404	45.164	1.00	32.88
ATOM	3170	N	SER	421	57.571	40.488	45.991	1.00	31.19
ATOM	3171	CA	SER	421	56.697	41.549	45.499	1.00	30.32
ATOM	3172	CB	SER	421	55.345	40.970	45.077	1.00	32.75
ATOM	3173	OG	SER	421	54.882	40.006	46.012	1.00	36.22
ATOM	3174	C	SER	421	56.497	42.603	46.559	1.00	30.53
ATOM	3175	O	SER	421	56.132	43.744	46.264	1.00	31.77
ATOM	3176	N	LEU	422	56.738	42.221	47.805	1.00	30.40
ATOM	3177	CA	LEU	422	56.604	43.151	48.917	1.00	29.35
ATOM	3178	CB	LEU	422	55.254	42.986	49.622	1.00	30.25
ATOM	3179	CG	LEU	422	55.121	43.842	50.888	1.00	29.90
ATOM	3180	CD1	LEU	422	55.036	45.319	50.512	1.00	28.81
ATOM	3181	CD2	LEU	422	53.893	43.415	51.663	1.00	31.47
ATOM	3182	C	LEU	422	57.706	42.893	49.920	1.00	29.76
ATOM	3183	O	LEU	422	57.782	41.808	50.501	1.00	29.18
ATOM	3184	N	THR	423	58.551	43.896	50.137	1.00	29.22
ATOM	3185	CA	THR	423	59.640	43.755	51.080	1.00	29.16
ATOM	3186	CB	THR	423	60.979	43.717	50.349	1.00	30.73
ATOM	3187	OG1	THR	423	60.952	42.685	49.357	1.00	26.80
ATOM	3188	CG2	THR	423	62.103	43.462	51.326	1.00	29.57
ATOM	3189	C	THR	423	59.671	44.904	52.076	1.00	32.07
ATOM	3190	O	THR	423	59.665	46.070	51.701	1.00	34.06
ATOM	3191	N	LEU	424	59.697	44.572	53.356	1.00	33.32
ATOM	3192	CA	LEU	424	59.757	45.588	54.386	1.00	32.23
ATOM	3193	CB	LEU	424	58.432	45.680	55.131	1.00	31.70
ATOM	3194	CG	LEU	424	57.199	45.898	54.266	1.00	31.60
ATOM	3195	CD1	LEU	424	56.001	46.055	55.196	1.00	32.03
ATOM	3196	CD2	LEU	424	57.374	47.131	53.384	1.00	30.01
ATOM	3197	C	LEU	424	60.830	45.109	55.321	1.00	32.73
ATOM	3198	O	LEU	424	60.655	44.093	55.990	1.00	33.11
ATOM	3199	N	GLN	425	61.941	45.834	55.367	1.00	35.85
ATOM	3200	CA	GLN	425	63.054	45.448	56.225	1.00	38.67
ATOM	3201	CB	GLN	425	64.051	44.596	55.427	1.00	39.34
ATOM	3202	CG	GLN	425	64.565	45.265	54.172	1.00	41.63
ATOM	3203	CD	GLN	425	65.575	44.410	53.435	1.00	44.59
ATOM	3204	OE1	GLN	425	65.325	43.229	53.160	1.00	45.28
ATOM	3205	NE2	GLN	425	66.723	44.999	53.105	1.00	42.97
ATOM	3206	C	GLN	425	63.794	46.613	56.891	1.00	39.68
ATOM	3207	O	GLN	425	63.935	47.704	56.320	1.00	40.17
ATOM	3208	N	GLY	426	64.258	46.348	58.112	1.00	40.10
ATOM	3209	CA	GLY	426	64.992	47.323	58.899	1.00	39.31
ATOM	3210	C	GLY	426	64.228	48.585	59.233	1.00	39.60
ATOM	3211	O	GLY	426	64.839	49.576	59.615	1.00	41.24
ATOM	3212	N	LEU	427	62.906	48.562	59.114	1.00	38.98
ATOM	3213	CA	LEU	427	62.117	49.759	59.390	1.00	39.49
ATOM	3214	CB	LEU	427	60.808	49.704	58.613	1.00	39.56
ATOM	3215	CG	LEU	427	60.970	49.266	57.157	1.00	39.73
ATOM	3216	CD1	LEU	427	59.601	49.006	56.567	1.00	39.64
ATOM	3217	CD2	LEU	427	61.711	50.331	56.365	1.00	38.74
ATOM	3218	C	LEU	427	61.817	49.990	60.866	1.00	40.51
ATOM	3219	O	LEU	427	62.114	49.149	61.727	1.00	40.55
ATOM	3220	N	GLY	428	61.228	51.148	61.149	1.00	40.84
ATOM	3221	CA	GLY	428	60.884	51.493	62.514	1.00	38.84
ATOM	3222	C	GLY	428	59.381	51.565	62.697	1.00	40.06
ATOM	3223	O	GLY	428	58.897	51.957	63.761	1.00	40.32
ATOM	3224	N	ILE	429	58.630	51.179	61.669	1.00	39.38
ATOM	3225	CA	ILE	429	57.178	51.230	61.759	1.00	38.33
ATOM	3226	CB	ILE	429	56.518	50.853	60.428	1.00	37.87
ATOM	3227	CG2	ILE	429	56.897	51.876	59.371	1.00	38.44
ATOM	3228	CG1	ILE	429	56.932	49.444	60.002	1.00	37.36
ATOM	3229	CD1	ILE	429	56.211	48.957	58.741	1.00	34.27

ATOM	3230	C	ILE	429	56.615	50.343	62.865	1.00	38.00
ATOM	3231	O	ILE	429	57.205	49.313	63.219	1.00	35.51
ATOM	3232	N	SER	430	55.472	50.758	63.412	1.00	37.06
ATOM	3233	CA	SER	430	54.826	50.013	64.480	1.00	36.12
ATOM	3234	CB	SER	430	54.293	50.968	65.531	1.00	37.07
ATOM	3235	OG	SER	430	55.382	51.538	66.235	1.00	37.62
ATOM	3236	C	SER	430	53.729	49.107	63.960	1.00	35.48
ATOM	3237	O	SER	430	53.370	48.132	64.612	1.00	35.19
ATOM	3238	N	TRP	431	53.204	49.426	62.781	1.00	36.17
ATOM	3239	CA	TRP	431	52.190	48.588	62.132	1.00	37.40
ATOM	3240	CB	TRP	431	50.798	48.784	62.763	1.00	38.03
ATOM	3241	CG	TRP	431	50.242	50.167	62.666	1.00	38.99
ATOM	3242	CD2	TRP	431	50.377	51.200	63.643	1.00	37.91
ATOM	3243	CE2	TRP	431	49.793	52.370	63.099	1.00	36.90
ATOM	3244	CE3	TRP	431	50.944	51.255	64.922	1.00	37.49
ATOM	3245	CD1	TRP	431	49.588	50.726	61.600	1.00	39.59
ATOM	3246	NE1	TRP	431	49.318	52.054	61.854	1.00	38.21
ATOM	3247	CZ2	TRP	431	49.762	53.581	63.790	1.00	36.66
ATOM	3248	CZ3	TRP	431	50.913	52.463	65.610	1.00	40.07
ATOM	3249	CH2	TRP	431	50.325	53.612	65.040	1.00	37.72
ATOM	3250	C	TRP	431	52.177	48.900	60.636	1.00	38.01
ATOM	3251	O	TRP	431	52.692	49.925	60.205	1.00	38.72
ATOM	3252	N	LEU	432	51.605	48.014	59.835	1.00	38.11
ATOM	3253	CA	LEU	432	51.596	48.239	58.402	1.00	37.62
ATOM	3254	CB	LEU	432	51.281	46.929	57.692	1.00	37.35
ATOM	3255	CG	LEU	432	52.243	45.818	58.122	1.00	34.41
ATOM	3256	CD1	LEU	432	51.976	44.598	57.284	1.00	37.13
ATOM	3257	CD2	LEU	432	53.680	46.269	57.959	1.00	32.05
ATOM	3258	C	LEU	432	50.657	49.344	57.940	1.00	38.77
ATOM	3259	O	LEU	432	51.105	50.356	57.384	1.00	39.52
ATOM	3260	N	GLY	433	49.359	49.154	58.144	1.00	38.86
ATOM	3261	CA	GLY	433	48.411	50.180	57.742	1.00	38.46
ATOM	3262	C	GLY	433	48.067	50.179	56.267	1.00	40.43
ATOM	3263	O	GLY	433	47.531	51.159	55.742	1.00	39.11
ATOM	3264	N	LEU	434	48.393	49.083	55.588	1.00	41.72
ATOM	3265	CA	LEU	434	48.091	48.942	54.166	1.00	44.07
ATOM	3266	CB	LEU	434	49.052	47.922	53.552	1.00	41.25
ATOM	3267	CG	LEU	434	50.539	48.289	53.655	1.00	41.54
ATOM	3268	CD1	LEU	434	51.399	47.068	53.381	1.00	39.57
ATOM	3269	CD2	LEU	434	50.872	49.397	52.668	1.00	40.90
ATOM	3270	C	LEU	434	46.636	48.443	54.092	1.00	46.14
ATOM	3271	O	LEU	434	46.341	47.409	53.483	1.00	45.75
ATOM	3272	N	ARG	435	45.734	49.201	54.716	1.00	47.92
ATOM	3273	CA	ARG	435	44.319	48.834	54.812	1.00	50.23
ATOM	3274	CB	ARG	435	43.540	49.923	55.549	1.00	54.76
ATOM	3275	CG	ARG	435	43.562	51.270	54.874	1.00	59.93
ATOM	3276	CD	ARG	435	42.595	52.231	55.537	1.00	64.22
ATOM	3277	NE	ARG	435	42.370	53.382	54.672	1.00	71.06
ATOM	3278	CZ	ARG	435	41.303	54.170	54.722	1.00	73.22
ATOM	3279	NH1	ARG	435	40.338	53.940	55.611	1.00	74.09
ATOM	3280	NH2	ARG	435	41.196	55.180	53.864	1.00	74.84
ATOM	3281	C	ARG	435	43.550	48.452	53.559	1.00	49.26
ATOM	3282	O	ARG	435	42.602	47.682	53.649	1.00	49.02
ATOM	3283	N	SER	436	43.937	48.970	52.398	1.00	48.80
ATOM	3284	CA	SER	436	43.236	48.633	51.161	1.00	47.08
ATOM	3285	CB	SER	436	43.154	49.855	50.251	1.00	49.11
ATOM	3286	OG	SER	436	42.243	50.807	50.760	1.00	51.09
ATOM	3287	C	SER	436	43.851	47.481	50.374	1.00	46.81
ATOM	3288	O	SER	436	43.266	47.009	49.396	1.00	48.99
ATOM	3289	N	LEU	437	45.019	47.014	50.801	1.00	46.11
ATOM	3290	CA	LEU	437	45.710	45.940	50.096	1.00	44.52

ATOM	3291	CB	LEU	437	47.107	45.758	50.674	1.00	42.22
ATOM	3292	CG	LEU	437	47.982	44.747	49.937	1.00	40.49
ATOM	3293	CD1	LEU	437	48.241	45.250	48.519	1.00	36.99
ATOM	3294	CD2	LEU	437	49.290	44.552	50.698	1.00	39.32
ATOM	3295	C	LEU	437	44.976	44.610	50.132	1.00	45.78
ATOM	3296	O	LEU	437	44.915	43.955	51.174	1.00	45.88
ATOM	3297	N	ARG	438	44.436	44.194	48.993	1.00	46.68
ATOM	3298	CA	ARG	438	43.715	42.928	48.949	1.00	49.57
ATOM	3299	CB	ARG	438	42.283	43.137	48.435	1.00	51.68
ATOM	3300	CG	ARG	438	42.228	43.703	47.025	1.00	57.84
ATOM	3301	CD	ARG	438	41.034	43.180	46.234	1.00	62.85
ATOM	3302	NE	ARG	438	41.190	43.425	44.800	1.00	64.06
ATOM	3303	CZ	ARG	438	41.115	44.625	44.233	1.00	65.00
ATOM	3304	NH1	ARG	438	40.874	45.700	44.978	1.00	63.57
ATOM	3305	NH2	ARG	438	41.305	44.753	42.925	1.00	65.53
ATOM	3306	C	ARG	438	44.404	41.880	48.081	1.00	48.81
ATOM	3307	O	ARG	438	43.934	40.743	47.998	1.00	49.66
ATOM	3308	N	GLU	439	45.504	42.245	47.425	1.00	47.06
ATOM	3309	CA	GLU	439	46.194	41.273	46.577	1.00	46.12
ATOM	3310	CB	GLU	439	45.407	41.026	45.280	1.00	45.20
ATOM	3311	CG	GLU	439	46.269	40.369	44.188	1.00	48.25
ATOM	3312	CD	GLU	439	45.546	40.096	42.873	1.00	49.06
ATOM	3313	OE1	GLU	439	44.639	40.867	42.494	1.00	52.99
ATOM	3314	OE2	GLU	439	45.910	39.112	42.199	1.00	49.12
ATOM	3315	C	GLU	439	47.649	41.519	46.180	1.00	44.21
ATOM	3316	O	GLU	439	48.061	42.634	45.860	1.00	43.68
ATOM	3317	N	LEU	440	48.403	40.429	46.192	1.00	41.98
ATOM	3318	CA	LEU	440	49.789	40.407	45.768	1.00	40.35
ATOM	3319	CB	LEU	440	50.687	39.888	46.885	1.00	38.01
ATOM	3320	CG	LEU	440	50.834	40.836	48.079	1.00	36.14
ATOM	3321	CD1	LEU	440	51.618	40.156	49.172	1.00	36.28
ATOM	3322	CD2	LEU	440	51.549	42.102	47.643	1.00	37.02
ATOM	3323	C	LEU	440	49.724	39.412	44.618	1.00	40.73
ATOM	3324	O	LEU	440	49.757	38.204	44.830	1.00	42.71
ATOM	3325	N	GLY	441	49.590	39.932	43.402	1.00	41.24
ATOM	3326	CA	GLY	441	49.472	39.088	42.223	1.00	41.63
ATOM	3327	C	GLY	441	50.400	37.892	42.136	1.00	42.55
ATOM	3328	O	GLY	441	50.009	36.821	41.668	1.00	43.43
ATOM	3329	N	SER	442	51.641	38.076	42.563	1.00	41.02
ATOM	3330	CA	SER	442	52.613	37.002	42.531	1.00	40.92
ATOM	3331	CB	SER	442	53.030	36.683	41.092	1.00	41.27
ATOM	3332	OG	SER	442	53.645	37.802	40.492	1.00	45.36
ATOM	3333	C	SER	442	53.808	37.447	43.338	1.00	40.20
ATOM	3334	O	SER	442	53.890	38.613	43.742	1.00	40.30
ATOM	3335	N	GLY	443	54.728	36.518	43.582	1.00	38.65
ATOM	3336	CA	GLY	443	55.901	36.834	44.369	1.00	37.83
ATOM	3337	C	GLY	443	55.631	36.603	45.844	1.00	39.08
ATOM	3338	O	GLY	443	54.475	36.493	46.268	1.00	39.98
ATOM	3339	N	LEU	444	56.696	36.525	46.631	1.00	37.91
ATOM	3340	CA	LEU	444	56.567	36.310	48.053	1.00	37.00
ATOM	3341	CB	LEU	444	57.694	35.415	48.538	1.00	38.41
ATOM	3342	CG	LEU	444	57.537	33.963	48.088	1.00	42.05
ATOM	3343	CD1	LEU	444	58.864	33.394	47.609	1.00	45.89
ATOM	3344	CD2	LEU	444	56.983	33.161	49.241	1.00	42.56
ATOM	3345	C	LEU	444	56.630	37.640	48.764	1.00	38.87
ATOM	3346	O	LEU	444	56.975	38.656	48.162	1.00	42.31
ATOM	3347	N	ALA	445	56.276	37.632	50.044	1.00	37.35
ATOM	3348	CA	ALA	445	56.310	38.821	50.868	1.00	34.33
ATOM	3349	CB	ALA	445	54.996	39.004	51.575	1.00	34.87
ATOM	3350	C	ALA	445	57.413	38.595	51.881	1.00	34.94
ATOM	3351	O	ALA	445	57.487	37.534	52.506	1.00	34.95

ATOM	3352	N	LEU	446	58.282	39.582	52.040	1.00	33.98
ATOM	3353	CA	LEU	446	59.366	39.457	52.990	1.00	32.14
ATOM	3354	CB	LEU	446	60.705	39.427	52.259	1.00	31.79
ATOM	3355	CG	LEU	446	61.968	39.387	53.128	1.00	35.26
ATOM	3356	CD1	LEU	446	61.878	38.262	54.154	1.00	35.34
ATOM	3357	CD2	LEU	446	63.183	39.202	52.237	1.00	35.63
ATOM	3358	C	LEU	446	59.302	40.627	53.946	1.00	34.42
ATOM	3359	O	LEU	446	59.372	41.787	53.526	1.00	36.09
ATOM	3360	N	ILE	447	59.148	40.316	55.233	1.00	34.59
ATOM	3361	CA	ILE	447	59.059	41.326	56.279	1.00	33.79
ATOM	3362	CB	ILE	447	57.617	41.456	56.770	1.00	33.38
ATOM	3363	CG2	ILE	447	57.528	42.521	57.846	1.00	34.06
ATOM	3364	CG1	ILE	447	56.699	41.770	55.588	1.00	32.75
ATOM	3365	CD1	ILE	447	55.245	42.062	55.994	1.00	34.78
ATOM	3366	C	ILE	447	59.944	40.889	57.438	1.00	35.09
ATOM	3367	O	ILE	447	59.622	39.931	58.147	1.00	36.39
ATOM	3368	N	HIS	448	61.061	41.574	57.643	1.00	34.59
ATOM	3369	CA	HIS	448	61.945	41.156	58.716	1.00	37.11
ATOM	3370	CB	HIS	448	62.853	40.028	58.223	1.00	39.27
ATOM	3371	CG	HIS	448	63.904	40.486	57.264	1.00	38.82
ATOM	3372	CD2	HIS	448	63.852	40.725	55.933	1.00	39.04
ATOM	3373	ND1	HIS	448	65.177	40.825	57.667	1.00	39.32
ATOM	3374	CE1	HIS	448	65.864	41.257	56.624	1.00	40.51
ATOM	3375	NE2	HIS	448	65.083	41.207	55.560	1.00	41.38
ATOM	3376	C	HIS	448	62.792	42.277	59.285	1.00	39.00
ATOM	3377	O	HIS	448	63.011	43.306	58.637	1.00	39.77
ATOM	3378	N	HIS	449	63.276	42.046	60.502	1.00	39.63
ATOM	3379	CA	HIS	449	64.091	43.008	61.222	1.00	40.27
ATOM	3380	CB	HIS	449	65.477	43.120	60.594	1.00	40.23
ATOM	3381	CG	HIS	449	66.346	41.940	60.892	1.00	45.12
ATOM	3382	CD2	HIS	449	67.248	41.725	61.879	1.00	45.97
ATOM	3383	ND1	HIS	449	66.260	40.757	60.188	1.00	46.84
ATOM	3384	CE1	HIS	449	67.071	39.864	60.731	1.00	47.26
ATOM	3385	NE2	HIS	449	67.682	40.426	61.761	1.00	46.02
ATOM	3386	C	HIS	449	63.439	44.370	61.362	1.00	39.67
ATOM	3387	O	HIS	449	64.067	45.410	61.157	1.00	39.10
ATOM	3388	N	ASN	450	62.157	44.339	61.711	1.00	39.45
ATOM	3389	CA	ASN	450	61.371	45.544	61.965	1.00	38.40
ATOM	3390	CB	ASN	450	60.119	45.525	61.110	1.00	37.35
ATOM	3391	CG	ASN	450	60.442	45.445	59.639	1.00	35.81
ATOM	3392	OD1	ASN	450	61.142	46.313	59.106	1.00	35.66
ATOM	3393	ND2	ASN	450	59.942	44.407	58.971	1.00	32.14
ATOM	3394	C	ASN	450	61.034	45.410	63.445	1.00	38.45
ATOM	3395	O	ASN	450	60.003	44.846	63.816	1.00	38.05
ATOM	3396	N	THR	451	61.948	45.908	64.274	1.00	38.23
ATOM	3397	CA	THR	451	61.881	45.839	65.729	1.00	39.20
ATOM	3398	CB	THR	451	62.996	46.689	66.323	1.00	40.04
ATOM	3399	OG1	THR	451	64.247	46.203	65.835	1.00	44.58
ATOM	3400	CG2	THR	451	62.984	46.622	67.840	1.00	38.85
ATOM	3401	C	THR	451	60.590	46.192	66.463	1.00	40.85
ATOM	3402	O	THR	451	60.184	45.491	67.400	1.00	40.47
ATOM	3403	N	HIS	452	59.955	47.281	66.058	1.00	40.04
ATOM	3404	CA	HIS	452	58.745	47.724	66.721	1.00	40.12
ATOM	3405	CB	HIS	452	58.771	49.249	66.842	1.00	41.64
ATOM	3406	CG	HIS	452	60.048	49.797	67.401	1.00	42.19
ATOM	3407	CD2	HIS	452	61.034	50.523	66.823	1.00	42.10
ATOM	3408	ND1	HIS	452	60.404	49.655	68.726	1.00	41.64
ATOM	3409	CE1	HIS	452	61.551	50.277	68.941	1.00	42.19
ATOM	3410	NE2	HIS	452	61.955	50.813	67.803	1.00	41.89
ATOM	3411	C	HIS	452	57.504	47.316	65.951	1.00	40.45
ATOM	3412	O	HIS	452	56.407	47.801	66.231	1.00	41.14

ATOM	3413	N	LEU	453	57.660	46.424	64.984	1.00	40.04
ATOM	3414	CA	LEU	453	56.521	46.049	64.167	1.00	40.19
ATOM	3415	CB	LEU	453	57.001	45.606	62.782	1.00	37.00
ATOM	3416	CG	LEU	453	55.893	45.347	61.759	1.00	37.34
ATOM	3417	CD1	LEU	453	55.194	46.659	61.397	1.00	32.28
ATOM	3418	CD2	LEU	453	56.490	44.686	60.516	1.00	35.69
ATOM	3419	C	LEU	453	55.597	44.993	64.746	1.00	40.85
ATOM	3420	O	LEU	453	56.018	43.883	65.038	1.00	41.66
ATOM	3421	N	CYS	454	54.333	45.360	64.925	1.00	43.03
ATOM	3422	CA	CYS	454	53.324	44.426	65.404	1.00	45.80
ATOM	3423	C	CYS	454	52.311	44.337	64.277	1.00	47.23
ATOM	3424	O	CYS	454	52.589	44.766	63.160	1.00	50.06
ATOM	3425	CB	CYS	454	52.647	44.928	66.682	1.00	48.08
ATOM	3426	SG	CYS	454	53.699	44.807	68.162	1.00	52.71
ATOM	3427	N	PHE	455	51.144	43.776	64.554	1.00	46.70
ATOM	3428	CA	PHE	455	50.107	43.660	63.537	1.00	46.11
ATOM	3429	CB	PHE	455	49.487	45.025	63.255	1.00	44.91
ATOM	3430	CG	PHE	455	48.892	45.645	64.460	1.00	45.40
ATOM	3431	CD1	PHE	455	49.692	46.348	65.358	1.00	46.60
ATOM	3432	CD2	PHE	455	47.555	45.440	64.763	1.00	45.00
ATOM	3433	CE1	PHE	455	49.169	46.831	66.545	1.00	48.01
ATOM	3434	CE2	PHE	455	47.015	45.916	65.947	1.00	46.34
ATOM	3435	CZ	PHE	455	47.819	46.613	66.844	1.00	47.91
ATOM	3436	C	PHE	455	50.564	43.033	62.244	1.00	45.88
ATOM	3437	O	PHE	455	50.200	43.484	61.168	1.00	46.84
ATOM	3438	N	VAL	456	51.367	41.989	62.355	1.00	47.26
ATOM	3439	CA	VAL	456	51.833	41.263	61.191	1.00	49.14
ATOM	3440	CB	VAL	456	53.332	40.892	61.315	1.00	50.57
ATOM	3441	CG1	VAL	456	53.768	40.038	60.121	1.00	48.77
ATOM	3442	CG2	VAL	456	54.174	42.159	61.412	1.00	49.21
ATOM	3443	C	VAL	456	50.998	39.988	61.183	1.00	51.32
ATOM	3444	O	VAL	456	50.487	39.569	60.137	1.00	51.84
ATOM	3445	N	HIS	457	50.844	39.387	62.365	1.00	52.85
ATOM	3446	CA	HIS	457	50.080	38.149	62.499	1.00	54.27
ATOM	3447	CB	HIS	457	50.398	37.435	63.830	1.00	57.53
ATOM	3448	CG	HIS	457	49.938	38.172	65.056	1.00	62.48
ATOM	3449	CD2	HIS	457	48.920	37.921	65.917	1.00	63.06
ATOM	3450	ND1	HIS	457	50.562	39.310	65.527	1.00	63.53
ATOM	3451	CE1	HIS	457	49.950	39.726	66.622	1.00	63.21
ATOM	3452	NE2	HIS	457	48.951	38.903	66.880	1.00	63.61
ATOM	3453	C	HIS	457	48.583	38.390	62.389	1.00	52.92
ATOM	3454	O	HIS	457	47.819	37.448	62.190	1.00	52.93
ATOM	3455	N	THR	458	48.173	39.652	62.505	1.00	51.57
ATOM	3456	CA	THR	458	46.760	40.016	62.422	1.00	49.96
ATOM	3457	CB	THR	458	46.488	41.361	63.099	1.00	50.57
ATOM	3458	OG1	THR	458	47.275	42.382	62.468	1.00	48.76
ATOM	3459	CG2	THR	458	46.835	41.290	64.576	1.00	50.84
ATOM	3460	C	THR	458	46.275	40.127	60.984	1.00	49.72
ATOM	3461	O	THR	458	45.078	40.284	60.742	1.00	49.69
ATOM	3462	N	VAL	459	47.204	40.055	60.037	1.00	47.78
ATOM	3463	CA	VAL	459	46.862	40.152	58.626	1.00	46.18
ATOM	3464	CB	VAL	459	47.970	40.901	57.836	1.00	45.27
ATOM	3465	CG1	VAL	459	47.655	40.896	56.357	1.00	41.77
ATOM	3466	CG2	VAL	459	48.088	42.327	58.340	1.00	42.75
ATOM	3467	C	VAL	459	46.649	38.768	58.008	1.00	47.65
ATOM	3468	O	VAL	459	47.468	37.862	58.174	1.00	47.15
ATOM	3469	N	PRO	460	45.532	38.590	57.281	1.00	48.28
ATOM	3470	CD	PRO	460	44.465	39.590	57.079	1.00	47.27
ATOM	3471	CA	PRO	460	45.188	37.323	56.626	1.00	47.47
ATOM	3472	CB	PRO	460	43.693	37.475	56.388	1.00	47.62
ATOM	3473	CG	PRO	460	43.589	38.932	56.022	1.00	46.72

ATOM	3474	C	PRO	460	45.965	37.157	55.318	1.00	47.25
ATOM	3475	O	PRO	460	45.376	37.114	54.234	1.00	47.13
ATOM	3476	N	TRP	461	47.285	37.052	55.427	1.00	45.76
ATOM	3477	CA	TRP	461	48.151	36.934	54.258	1.00	44.54
ATOM	3478	CB	TRP	461	49.569	36.609	54.717	1.00	40.95
ATOM	3479	CG	TRP	461	50.152	37.709	55.539	1.00	40.30
ATOM	3480	CD2	TRP	461	50.621	38.978	55.060	1.00	40.35
ATOM	3481	CE2	TRP	461	51.053	39.716	56.185	1.00	39.87
ATOM	3482	CE3	TRP	461	50.718	39.562	53.789	1.00	39.46
ATOM	3483	CD1	TRP	461	50.310	37.731	56.897	1.00	38.03
ATOM	3484	NE1	TRP	461	50.850	38.934	57.293	1.00	38.31
ATOM	3485	CZ2	TRP	461	51.576	41.008	56.075	1.00	39.81
ATOM	3486	CZ3	TRP	461	51.237	40.847	53.681	1.00	38.47
ATOM	3487	CH2	TRP	461	51.660	41.555	54.818	1.00	40.35
ATOM	3488	C	TRP	461	47.707	35.960	53.166	1.00	45.92
ATOM	3489	O	TRP	461	47.841	36.254	51.973	1.00	42.98
ATOM	3490	N	ASP	462	47.172	34.810	53.563	1.00	48.29
ATOM	3491	CA	ASP	462	46.713	33.817	52.593	1.00	50.04
ATOM	3492	CB	ASP	462	46.136	32.615	53.327	1.00	54.39
ATOM	3493	CG	ASP	462	47.196	31.833	54.068	1.00	60.56
ATOM	3494	OD1	ASP	462	46.845	31.154	55.064	1.00	63.99
ATOM	3495	OD2	ASP	462	48.380	31.890	53.648	1.00	62.32
ATOM	3496	C	ASP	462	45.676	34.388	51.631	1.00	47.95
ATOM	3497	O	ASP	462	45.593	33.979	50.482	1.00	47.15
ATOM	3498	N	GLN	463	44.879	35.327	52.112	1.00	47.85
ATOM	3499	CA	GLN	463	43.868	35.951	51.279	1.00	49.93
ATOM	3500	CB	GLN	463	42.964	36.862	52.132	1.00	52.77
ATOM	3501	CG	GLN	463	41.948	36.126	53.015	1.00	57.25
ATOM	3502	CD	GLN	463	41.022	37.074	53.790	1.00	60.95
ATOM	3503	OE1	GLN	463	40.433	38.005	53.219	1.00	62.40
ATOM	3504	NE2	GLN	463	40.880	36.830	55.095	1.00	62.71
ATOM	3505	C	GLN	463	44.504	36.766	50.138	1.00	49.27
ATOM	3506	O	GLN	463	43.979	36.789	49.026	1.00	49.51
ATOM	3507	N	LEU	464	45.636	37.418	50.405	1.00	47.31
ATOM	3508	CA	LEU	464	46.304	38.237	49.394	1.00	46.23
ATOM	3509	CB	LEU	464	47.310	39.169	50.068	1.00	46.42
ATOM	3510	CG	LEU	464	46.803	39.973	51.266	1.00	47.92
ATOM	3511	CD1	LEU	464	47.859	40.972	51.695	1.00	46.98
ATOM	3512	CD2	LEU	464	45.526	40.685	50.896	1.00	49.82
ATOM	3513	C	LEU	464	47.012	37.480	48.257	1.00	45.85
ATOM	3514	O	LEU	464	47.095	37.977	47.129	1.00	45.77
ATOM	3515	N	PHE	465	47.524	36.290	48.542	1.00	44.21
ATOM	3516	CA	PHE	465	48.229	35.514	47.532	1.00	45.10
ATOM	3517	CB	PHE	465	49.029	34.400	48.203	1.00	42.93
ATOM	3518	CG	PHE	465	50.001	34.895	49.240	1.00	42.74
ATOM	3519	CD1	PHE	465	50.800	36.010	48.987	1.00	41.77
ATOM	3520	CD2	PHE	465	50.131	34.243	50.463	1.00	41.86
ATOM	3521	CE1	PHE	465	51.713	36.467	49.935	1.00	41.10
ATOM	3522	CE2	PHE	465	51.041	34.688	51.421	1.00	40.99
ATOM	3523	CZ	PHE	465	51.833	35.801	51.160	1.00	42.60
ATOM	3524	C	PHE	465	47.279	34.935	46.486	1.00	47.59
ATOM	3525	O	PHE	465	46.080	34.816	46.735	1.00	49.78
ATOM	3526	N	ARG	466	47.823	34.570	45.323	1.00	47.40
ATOM	3527	CA	ARG	466	47.036	34.028	44.221	1.00	45.90
ATOM	3528	CB	ARG	466	46.903	35.084	43.130	1.00	45.38
ATOM	3529	CG	ARG	466	46.126	36.321	43.557	1.00	46.15
ATOM	3530	CD	ARG	466	44.642	36.023	43.736	1.00	43.17
ATOM	3531	NE	ARG	466	43.879	37.221	44.084	1.00	42.43
ATOM	3532	CZ	ARG	466	43.744	37.693	45.321	1.00	41.90
ATOM	3533	NH1	ARG	466	44.318	37.068	46.337	1.00	38.17
ATOM	3534	NH2	ARG	466	43.035	38.795	45.544	1.00	41.69

ATOM	3535	C	ARG	466	47.551	32.724	43.590	1.00	47.53
ATOM	3536	O	ARG	466	46.932	32.200	42.660	1.00	48.19
ATOM	3537	N	ASN	467	48.682	32.209	44.064	1.00	47.38
ATOM	3538	CA	ASN	467	49.220	30.955	43.535	1.00	47.50
ATOM	3539	CB	ASN	467	50.154	31.209	42.334	1.00	48.16
ATOM	3540	CG	ASN	467	51.524	31.725	42.736	1.00	50.64
ATOM	3541	OD1	ASN	467	52.339	30.991	43.311	1.00	52.47
ATOM	3542	ND2	ASN	467	51.793	32.990	42.425	1.00	46.93
ATOM	3543	C	ASN	467	49.924	30.199	44.668	1.00	46.88
ATOM	3544	O	ASN	467	50.341	30.802	45.659	1.00	46.18
ATOM	3545	N	PRO	468	50.063	28.869	44.534	1.00	47.46
ATOM	3546	CD	PRO	468	49.835	28.116	43.291	1.00	46.51
ATOM	3547	CA	PRO	468	50.693	28.003	45.542	1.00	48.63
ATOM	3548	CB	PRO	468	50.617	26.610	44.914	1.00	48.24
ATOM	3549	CG	PRO	468	49.584	26.747	43.814	1.00	47.11
ATOM	3550	C	PRO	468	52.116	28.344	45.930	1.00	49.84
ATOM	3551	O	PRO	468	52.572	27.957	46.999	1.00	52.80
ATOM	3552	N	HIS	469	52.814	29.066	45.065	1.00	50.04
ATOM	3553	CA	HIS	469	54.199	29.409	45.318	1.00	49.71
ATOM	3554	CB	HIS	469	54.940	29.548	43.988	1.00	53.11
ATOM	3555	CG	HIS	469	55.012	28.276	43.201	1.00	54.91
ATOM	3556	CD2	HIS	469	54.448	27.924	42.021	1.00	54.62
ATOM	3557	ND1	HIS	469	55.737	27.181	43.622	1.00	56.43
ATOM	3558	CE1	HIS	469	55.620	26.211	42.733	1.00	56.70
ATOM	3559	NE2	HIS	469	54.843	26.636	41.752	1.00	55.63
ATOM	3560	C	HIS	469	54.423	30.653	46.154	1.00	48.30
ATOM	3561	O	HIS	469	55.567	31.030	46.394	1.00	48.74
ATOM	3562	N	GLN	470	53.349	31.287	46.610	1.00	47.55
ATOM	3563	CA	GLN	470	53.479	32.506	47.414	1.00	46.16
ATOM	3564	CB	GLN	470	52.433	33.535	46.993	1.00	45.94
ATOM	3565	CG	GLN	470	52.547	34.014	45.560	1.00	47.79
ATOM	3566	CD	GLN	470	51.472	35.034	45.218	1.00	48.54
ATOM	3567	OE1	GLN	470	50.320	34.677	44.971	1.00	48.75
ATOM	3568	NE2	GLN	470	51.840	36.309	45.223	1.00	44.96
ATOM	3569	C	GLN	470	53.331	32.255	48.909	1.00	46.20
ATOM	3570	O	GLN	470	52.631	31.331	49.333	1.00	47.30
ATOM	3571	N	ALA	471	53.972	33.107	49.702	1.00	44.42
ATOM	3572	CA	ALA	471	53.923	33.000	51.150	1.00	43.97
ATOM	3573	CB	ALA	471	54.650	31.745	51.607	1.00	43.76
ATOM	3574	C	ALA	471	54.588	34.219	51.763	1.00	44.57
ATOM	3575	O	ALA	471	55.245	35.000	51.071	1.00	42.63
ATOM	3576	N	LEU	472	54.417	34.377	53.069	1.00	42.98
ATOM	3577	CA	LEU	472	55.031	35.484	53.767	1.00	41.66
ATOM	3578	CB	LEU	472	54.049	36.128	54.746	1.00	41.67
ATOM	3579	CG	LEU	472	54.740	37.049	55.766	1.00	42.01
ATOM	3580	CD1	LEU	472	55.350	38.268	55.051	1.00	40.33
ATOM	3581	CD2	LEU	472	53.745	37.477	56.824	1.00	40.11
ATOM	3582	C	LEU	472	56.215	34.965	54.549	1.00	41.03
ATOM	3583	O	LEU	472	56.069	34.034	55.330	1.00	42.94
ATOM	3584	N	LEU	473	57.388	35.553	54.336	1.00	41.80
ATOM	3585	CA	LEU	473	58.582	35.154	55.075	1.00	40.99
ATOM	3586	CB	LEU	473	59.789	35.020	54.144	1.00	39.87
ATOM	3587	CG	LEU	473	59.554	34.118	52.927	1.00	40.65
ATOM	3588	CD1	LEU	473	60.896	33.717	52.334	1.00	40.09
ATOM	3589	CD2	LEU	473	58.754	32.884	53.324	1.00	38.13
ATOM	3590	C	LEU	473	58.792	36.271	56.078	1.00	41.31
ATOM	3591	O	LEU	473	58.828	37.441	55.712	1.00	41.51
ATOM	3592	N	HIS	474	58.929	35.910	57.349	1.00	43.35
ATOM	3593	CA	HIS	474	59.061	36.909	58.402	1.00	42.81
ATOM	3594	CB	HIS	474	57.668	37.264	58.888	1.00	42.99
ATOM	3595	CG	HIS	474	56.926	36.090	59.442	1.00	43.37

ATOM	3596	CD2	HIS	474	56.177	35.143	58.830	1.00	43.37
ATOM	3597	ND1	HIS	474	56.986	35.732	60.772	1.00	44.24
ATOM	3598	CE1	HIS	474	56.307	34.614	60.954	1.00	44.58
ATOM	3599	NE2	HIS	474	55.806	34.235	59.791	1.00	44.84
ATOM	3600	C	HIS	474	59.884	36.411	59.581	1.00	43.18
ATOM	3601	O	HIS	474	59.763	35.261	60.004	1.00	44.46
ATOM	3602	N	THR	475	60.703	37.292	60.132	1.00	42.59
ATOM	3603	CA	THR	475	61.533	36.920	61.257	1.00	41.62
ATOM	3604	CB	THR	475	62.673	35.973	60.802	1.00	42.51
ATOM	3605	OG1	THR	475	63.340	35.423	61.948	1.00	47.00
ATOM	3606	CG2	THR	475	63.685	36.724	59.953	1.00	42.92
ATOM	3607	C	THR	475	62.118	38.195	61.826	1.00	40.91
ATOM	3608	O	THR	475	62.245	39.188	61.117	1.00	41.61
ATOM	3609	N	ALA	476	62.458	38.171	63.110	1.00	41.19
ATOM	3610	CA	ALA	476	63.057	39.324	63.778	1.00	39.52
ATOM	3611	CB	ALA	476	64.442	39.612	63.178	1.00	37.39
ATOM	3612	C	ALA	476	62.221	40.615	63.814	1.00	40.28
ATOM	3613	O	ALA	476	62.774	41.719	63.790	1.00	41.36
ATOM	3614	N	ASN	477	60.897	40.493	63.846	1.00	39.57
ATOM	3615	CA	ASN	477	60.068	41.683	63.981	1.00	39.64
ATOM	3616	CB	ASN	477	58.836	41.609	63.084	1.00	40.20
ATOM	3617	CG	ASN	477	59.198	41.577	61.593	1.00	42.24
ATOM	3618	OD1	ASN	477	59.810	42.514	61.062	1.00	40.34
ATOM	3619	ND2	ASN	477	58.818	40.497	60.918	1.00	40.44
ATOM	3620	C	ASN	477	59.686	41.674	65.465	1.00	40.57
ATOM	3621	O	ASN	477	60.159	40.809	66.214	1.00	38.44
ATOM	3622	N	ARG	478	58.858	42.614	65.914	1.00	41.50
ATOM	3623	CA	ARG	478	58.506	42.630	67.329	1.00	40.80
ATOM	3624	CB	ARG	478	57.610	43.816	67.665	1.00	41.88
ATOM	3625	CG	ARG	478	57.488	44.006	69.161	1.00	42.92
ATOM	3626	CD	ARG	478	56.713	45.238	69.585	1.00	42.69
ATOM	3627	NE	ARG	478	56.840	45.392	71.035	1.00	46.73
ATOM	3628	CZ	ARG	478	56.010	46.080	71.814	1.00	44.48
ATOM	3629	NH1	ARG	478	54.959	46.702	71.302	1.00	45.76
ATOM	3630	NH2	ARG	478	56.239	46.144	73.115	1.00	45.84
ATOM	3631	C	ARG	478	57.796	41.341	67.724	1.00	42.21
ATOM	3632	O	ARG	478	56.818	40.941	67.094	1.00	42.14
ATOM	3633	N	PRO	479	58.276	40.672	68.783	1.00	43.41
ATOM	3634	CD	PRO	479	59.428	41.039	69.629	1.00	41.40
ATOM	3635	CA	PRO	479	57.658	39.415	69.238	1.00	43.35
ATOM	3636	CB	PRO	479	58.435	39.087	70.510	1.00	40.98
ATOM	3637	CG	PRO	479	59.794	39.717	70.254	1.00	41.03
ATOM	3638	C	PRO	479	56.155	39.544	69.494	1.00	45.50
ATOM	3639	O	PRO	479	55.686	40.533	70.060	1.00	45.59
ATOM	3640	N	GLU	480	55.401	38.539	69.072	1.00	49.19
ATOM	3641	CA	GLU	480	53.955	38.546	69.266	1.00	53.07
ATOM	3642	CB	GLU	480	53.330	37.306	68.617	1.00	54.18
ATOM	3643	CG	GLU	480	53.173	37.452	67.107	1.00	58.24
ATOM	3644	CD	GLU	480	52.862	36.146	66.416	1.00	61.65
ATOM	3645	OE1	GLU	480	51.961	35.426	66.897	1.00	63.71
ATOM	3646	OE2	GLU	480	53.514	35.845	65.387	1.00	63.95
ATOM	3647	C	GLU	480	53.551	38.642	70.734	1.00	53.99
ATOM	3648	O	GLU	480	52.522	39.223	71.054	1.00	55.14
ATOM	3649	N	ASP	481	54.361	38.086	71.627	1.00	55.81
ATOM	3650	CA	ASP	481	54.046	38.146	73.048	1.00	57.69
ATOM	3651	CB	ASP	481	54.943	37.196	73.850	1.00	59.27
ATOM	3652	CG	ASP	481	54.607	35.732	73.611	1.00	61.89
ATOM	3653	OD1	ASP	481	53.412	35.367	73.706	1.00	62.97
ATOM	3654	OD2	ASP	481	55.540	34.947	73.337	1.00	63.73
ATOM	3655	C	ASP	481	54.194	39.564	73.586	1.00	58.87
ATOM	3656	O	ASP	481	53.484	39.956	74.517	1.00	59.57

ATOM	3657	N	GLU	482	55.111	40.335	73.005	1.00	58.07
ATOM	3658	CA	GLU	482	55.322	41.707	73.442	1.00	57.66
ATOM	3659	CB	GLU	482	56.653	42.231	72.922	1.00	58.24
ATOM	3660	CG	GLU	482	57.814	41.616	73.634	1.00	61.21
ATOM	3661	CD	GLU	482	57.684	41.785	75.130	1.00	64.17
ATOM	3662	OE1	GLU	482	57.895	42.916	75.630	1.00	65.63
ATOM	3663	OE2	GLU	482	57.350	40.787	75.803	1.00	65.01
ATOM	3664	C	GLU	482	54.188	42.584	72.951	1.00	58.20
ATOM	3665	O	GLU	482	53.732	43.485	73.655	1.00	58.45
ATOM	3666	N	CYS	483	53.736	42.318	71.732	1.00	57.89
ATOM	3667	CA	CYS	483	52.638	43.082	71.167	1.00	58.21
ATOM	3668	C	CYS	483	51.434	42.873	72.084	1.00	59.50
ATOM	3669	O	CYS	483	50.901	43.828	72.657	1.00	58.80
ATOM	3670	CB	CYS	483	52.327	42.595	69.747	1.00	56.50
ATOM	3671	SG	CYS	483	53.718	42.813	68.586	1.00	54.37
ATOM	3672	N	VAL	484	51.028	41.614	72.231	1.00	59.47
ATOM	3673	CA	VAL	484	49.901	41.264	73.084	1.00	59.07
ATOM	3674	CB	VAL	484	49.638	39.742	73.037	1.00	60.26
ATOM	3675	CG1	VAL	484	48.555	39.356	74.038	1.00	61.90
ATOM	3676	CG2	VAL	484	49.218	39.339	71.626	1.00	58.82
ATOM	3677	C	VAL	484	50.190	41.710	74.518	1.00	58.07
ATOM	3678	O	VAL	484	49.300	42.180	75.228	1.00	56.65
ATOM	3679	N	GLY	485	51.446	41.580	74.928	1.00	57.91
ATOM	3680	CA	GLY	485	51.831	41.992	76.267	1.00	59.03
ATOM	3681	C	GLY	485	51.524	43.460	76.507	1.00	59.68
ATOM	3682	O	GLY	485	51.071	43.840	77.586	1.00	60.34
ATOM	3683	N	GLU	486	51.768	44.288	75.498	1.00	60.09
ATOM	3684	CA	GLU	486	51.502	45.717	75.602	1.00	60.59
ATOM	3685	CB	GLU	486	52.252	46.477	74.502	1.00	61.23
ATOM	3686	CG	GLU	486	52.540	47.925	74.838	1.00	62.83
ATOM	3687	CD	GLU	486	53.215	48.666	73.701	1.00	65.64
ATOM	3688	OE1	GLU	486	52.522	49.010	72.721	1.00	66.77
ATOM	3689	OE2	GLU	486	54.440	48.901	73.782	1.00	67.03
ATOM	3690	C	GLU	486	49.999	45.935	75.446	1.00	60.37
ATOM	3691	O	GLU	486	49.507	47.061	75.539	1.00	59.61
ATOM	3692	N	GLY	487	49.276	44.843	75.197	1.00	59.61
ATOM	3693	CA	GLY	487	47.835	44.927	75.028	1.00	58.40
ATOM	3694	C	GLY	487	47.369	45.243	73.614	1.00	57.71
ATOM	3695	O	GLY	487	46.177	45.471	73.392	1.00	58.87
ATOM	3696	N	LEU	488	48.292	45.248	72.655	1.00	56.03
ATOM	3697	CA	LEU	488	47.952	45.546	71.268	1.00	54.46
ATOM	3698	CB	LEU	488	49.218	45.866	70.473	1.00	52.69
ATOM	3699	CG	LEU	488	50.005	47.084	70.965	1.00	52.11
ATOM	3700	CD1	LEU	488	51.361	47.177	70.274	1.00	50.51
ATOM	3701	CD2	LEU	488	49.186	48.324	70.703	1.00	54.20
ATOM	3702	C	LEU	488	47.206	44.404	70.591	1.00	56.04
ATOM	3703	O	LEU	488	47.516	43.226	70.797	1.00	56.18
ATOM	3704	N	ALA	489	46.220	44.766	69.775	1.00	56.93
ATOM	3705	CA	ALA	489	45.414	43.791	69.045	1.00	57.23
ATOM	3706	CB	ALA	489	44.704	42.861	70.015	1.00	56.66
ATOM	3707	C	ALA	489	44.396	44.510	68.177	1.00	57.16
ATOM	3708	O	ALA	489	44.236	45.722	68.272	1.00	55.01
ATOM	3709	N	CYS	490	43.703	43.754	67.335	1.00	59.68
ATOM	3710	CA	CYS	490	42.704	44.331	66.446	1.00	61.86
ATOM	3711	C	CYS	490	41.547	44.932	67.230	1.00	65.58
ATOM	3712	O	CYS	490	41.165	44.415	68.284	1.00	66.33
ATOM	3713	CB	CYS	490	42.174	43.264	65.482	1.00	61.11
ATOM	3714	SG	CYS	490	43.394	42.650	64.269	1.00	60.72
ATOM	3715	N	HIS	491	40.994	46.026	66.712	1.00	68.46
ATOM	3716	CA	HIS	491	39.872	46.701	67.356	1.00	70.45
ATOM	3717	CB	HIS	491	39.443	47.912	66.529	1.00	71.52

ATOM	3718	CG	HIS	491	38.432	48.782	67.208	1.00	73.85
ATOM	3719	CD2	HIS	491	38.477	50.088	67.564	1.00	73.89
ATOM	3720	ND1	HIS	491	37.183	48.328	67.576	1.00	74.38
ATOM	3721	CE1	HIS	491	36.502	49.318	68.125	1.00	74.29
ATOM	3722	NE2	HIS	491	37.264	50.397	68.128	1.00	74.01
ATOM	3723	C	HIS	491	38.700	45.730	67.517	1.00	72.75
ATOM	3724	O	HIS	491	38.435	44.897	66.639	1.00	71.43
ATOM	3725	N	GLN	492	38.007	45.846	68.651	1.00	75.11
ATOM	3726	CA	GLN	492	36.876	44.978	68.979	1.00	76.23
ATOM	3727	CB	GLN	492	36.141	45.524	70.213	1.00	79.06
ATOM	3728	CG	GLN	492	35.318	44.487	70.987	1.00	82.25
ATOM	3729	CD	GLN	492	34.127	43.951	70.201	1.00	84.79
ATOM	3730	OE1	GLN	492	33.217	44.702	69.841	1.00	85.69
ATOM	3731	NE2	GLN	492	34.129	42.646	69.932	1.00	84.27
ATOM	3732	C	GLN	492	35.903	44.845	67.812	1.00	75.18
ATOM	3733	O	GLN	492	35.266	43.802	67.633	1.00	74.06
ATOM	3734	N	LEU	493	35.803	45.898	67.009	1.00	73.83
ATOM	3735	CA	LEU	493	34.895	45.884	65.878	1.00	74.17
ATOM	3736	CB	LEU	493	34.506	47.318	65.515	1.00	74.20
ATOM	3737	CG	LEU	493	33.341	47.339	64.712	1.00	74.76
ATOM	3738	C	LEU	493	35.456	45.156	64.647	1.00	74.56
ATOM	3739	O	LEU	493	34.791	45.088	63.613	1.00	74.80
ATOM	3740	N	CYS	494	36.674	44.620	64.745	1.00	73.90
ATOM	3741	CA	CYS	494	37.259	43.895	63.617	1.00	73.92
ATOM	3742	C	CYS	494	36.675	42.491	63.604	1.00	74.79
ATOM	3743	O	CYS	494	37.077	41.628	64.382	1.00	74.58
ATOM	3744	CB	CYS	494	38.787	43.817	63.727	1.00	73.15
ATOM	3745	SG	CYS	494	39.687	45.373	63.407	1.00	70.37
ATOM	3746	N	ALA	495	35.724	42.283	62.702	1.00	76.40
ATOM	3747	CA	ALA	495	35.006	41.021	62.551	1.00	77.39
ATOM	3748	CB	ALA	495	34.438	40.932	61.149	1.00	78.27
ATOM	3749	C	ALA	495	35.730	39.719	62.886	1.00	77.47
ATOM	3750	O	ALA	495	35.413	39.077	63.891	1.00	77.55
ATOM	3751	N	ARG	496	36.686	39.319	62.049	1.00	76.19
ATOM	3752	CA	ARG	496	37.391	38.060	62.274	1.00	75.09
ATOM	3753	CB	ARG	496	37.472	37.270	60.963	1.00	77.48
ATOM	3754	CG	ARG	496	36.656	35.975	60.967	1.00	79.11
ATOM	3755	CD	ARG	496	36.916	35.131	59.720	1.00	80.25
ATOM	3756	NE	ARG	496	36.382	35.803	58.462	1.00	82.56
ATOM	3757	CZ	ARG	496	34.891	35.920	58.474	1.00	83.50
ATOM	3758	C	ARG	496	38.783	38.171	62.888	1.00	73.32
ATOM	3759	O	ARG	496	39.644	37.330	62.636	1.00	73.14
ATOM	3760	N	GLY	497	38.995	39.196	63.707	1.00	71.64
ATOM	3761	CA	GLY	497	40.287	39.387	64.345	1.00	68.82
ATOM	3762	C	GLY	497	41.390	39.845	63.405	1.00	66.99
ATOM	3763	O	GLY	497	42.553	39.886	63.790	1.00	67.23
ATOM	3764	N	HIS	498	41.023	40.201	62.177	1.00	65.61
ATOM	3765	CA	HIS	498	41.987	40.646	61.171	1.00	64.32
ATOM	3766	CB	HIS	498	41.646	40.025	59.816	1.00	66.38
ATOM	3767	CG	HIS	498	41.612	38.531	59.832	1.00	67.04
ATOM	3768	CD2	HIS	498	42.128	37.639	60.709	1.00	66.05
ATOM	3769	ND1	HIS	498	40.993	37.791	58.846	1.00	68.48
ATOM	3770	CE1	HIS	498	41.131	36.506	59.115	1.00	69.68
ATOM	3771	NE2	HIS	498	41.815	36.386	60.240	1.00	69.46
ATOM	3772	C	HIS	498	42.037	42.158	61.010	1.00	62.27
ATOM	3773	O	HIS	498	41.003	42.812	60.867	1.00	62.26
ATOM	3774	N	CYS	499	43.250	42.704	61.009	1.00	59.39
ATOM	3775	CA	CYS	499	43.442	44.139	60.856	1.00	56.07
ATOM	3776	C	CYS	499	44.878	44.451	60.436	1.00	54.88
ATOM	3777	O	CYS	499	45.765	43.611	60.576	1.00	54.18
ATOM	3778	CB	CYS	499	43.121	44.842	62.171	1.00	53.82

ATOM	3779	SG	CYS	499	44.212	44.370	63.550	1.00	53.18
ATOM	3780	N	TRP	500	45.096	45.660	59.922	1.00	54.46
ATOM	3781	CA	TRP	500	46.422	46.096	59.483	1.00	54.35
ATOM	3782	CB	TRP	500	46.345	46.877	58.169	1.00	52.68
ATOM	3783	CG	TRP	500	45.967	46.062	56.991	1.00	52.13
ATOM	3784	CD2	TRP	500	46.855	45.330	56.134	1.00	52.51
ATOM	3785	CE2	TRP	500	46.059	44.678	55.170	1.00	52.41
ATOM	3786	CE3	TRP	500	48.246	45.163	56.090	1.00	52.09
ATOM	3787	CD1	TRP	500	44.710	45.834	56.525	1.00	51.98
ATOM	3788	NE1	TRP	500	44.754	45.002	55.432	1.00	53.67
ATOM	3789	CZ2	TRP	500	46.606	43.870	54.171	1.00	51.30
ATOM	3790	CZ3	TRP	500	48.792	44.360	55.094	1.00	51.18
ATOM	3791	CH2	TRP	500	47.970	43.724	54.148	1.00	51.05
ATOM	3792	C	TRP	500	47.048	47.002	60.519	1.00	55.36
ATOM	3793	O	TRP	500	48.159	47.500	60.328	1.00	55.37
ATOM	3794	N	GLY	501	46.324	47.234	61.607	1.00	56.86
ATOM	3795	CA	GLY	501	46.834	48.106	62.643	1.00	58.32
ATOM	3796	C	GLY	501	45.906	48.224	63.834	1.00	60.22
ATOM	3797	O	GLY	501	44.953	47.457	63.963	1.00	59.76
ATOM	3798	N	PRO	502	46.159	49.199	64.719	1.00	61.74
ATOM	3799	CD	PRO	502	47.338	50.076	64.639	1.00	61.18
ATOM	3800	CA	PRO	502	45.395	49.479	65.939	1.00	62.96
ATOM	3801	CB	PRO	502	46.227	50.565	66.626	1.00	62.80
ATOM	3802	CG	PRO	502	47.607	50.353	66.085	1.00	62.29
ATOM	3803	C	PRO	502	43.933	49.904	65.799	1.00	64.19
ATOM	3804	O	PRO	502	43.023	49.154	66.155	1.00	63.69
ATOM	3805	N	GLY	503	43.720	51.115	65.294	1.00	65.19
ATOM	3806	CA	GLY	503	42.376	51.657	65.168	1.00	67.81
ATOM	3807	C	GLY	503	41.284	50.832	64.511	1.00	69.48
ATOM	3808	O	GLY	503	41.498	49.675	64.149	1.00	69.49
ATOM	3809	N	PRO	504	40.078	51.412	64.359	1.00	70.50
ATOM	3810	CD	PRO	504	39.672	52.684	64.974	1.00	70.99
ATOM	3811	CA	PRO	504	38.918	50.755	63.742	1.00	70.28
ATOM	3812	CB	PRO	504	37.727	51.582	64.244	1.00	70.32
ATOM	3813	CG	PRO	504	38.272	52.375	65.398	1.00	70.99
ATOM	3814	C	PRO	504	39.036	50.827	62.225	1.00	69.41
ATOM	3815	O	PRO	504	38.374	50.083	61.499	1.00	69.42
ATOM	3816	N	THR	505	39.884	51.742	61.763	1.00	68.13
ATOM	3817	CA	THR	505	40.119	51.950	60.340	1.00	67.47
ATOM	3818	CB	THR	505	40.878	53.259	60.102	1.00	67.81
ATOM	3819	OG1	THR	505	40.220	54.325	60.796	1.00	67.46
ATOM	3820	CG2	THR	505	40.936	53.574	58.611	1.00	68.41
ATOM	3821	C	THR	505	40.947	50.834	59.714	1.00	67.11
ATOM	3822	O	THR	505	40.949	50.669	58.496	1.00	66.67
ATOM	3823	N	GLN	506	41.641	50.067	60.550	1.00	67.09
ATOM	3824	CA	GLN	506	42.513	49.000	60.074	1.00	66.20
ATOM	3825	CB	GLN	506	43.757	48.940	60.963	1.00	65.97
ATOM	3826	CG	GLN	506	44.438	50.292	61.156	1.00	65.10
ATOM	3827	CD	GLN	506	44.931	50.897	59.851	1.00	64.76
ATOM	3828	OE1	GLN	506	45.477	52.001	59.833	1.00	63.49
ATOM	3829	NE2	GLN	506	44.747	50.174	58.754	1.00	64.72
ATOM	3830	C	GLN	506	41.928	47.598	59.937	1.00	66.13
ATOM	3831	O	GLN	506	42.640	46.681	59.535	1.00	65.92
ATOM	3832	N	CYS	507	40.651	47.418	60.259	1.00	66.51
ATOM	3833	CA	CYS	507	40.043	46.094	60.147	1.00	67.92
ATOM	3834	C	CYS	507	40.079	45.584	58.711	1.00	69.10
ATOM	3835	O	CYS	507	40.336	46.351	57.786	1.00	68.98
ATOM	3836	CB	CYS	507	38.594	46.107	60.642	1.00	68.38
ATOM	3837	SG	CYS	507	38.351	46.532	62.400	1.00	67.08
ATOM	3838	N	VAL	508	39.804	44.293	58.534	1.00	71.60
ATOM	3839	CA	VAL	508	39.824	43.665	57.214	1.00	74.36

ATOM	3840	CB	VAL	508	41.094	42.802	57.046	1.00	74.35
ATOM	3841	CG1	VAL	508	41.169	42.249	55.637	1.00	73.86
ATOM	3842	CG2	VAL	508	42.325	43.620	57.372	1.00	74.61
ATOM	3843	C	VAL	508	38.618	42.760	56.926	1.00	76.71
ATOM	3844	O	VAL	508	37.993	42.232	57.846	1.00	76.96
ATOM	3845	N	ASN	509	38.320	42.583	55.637	1.00	78.89
ATOM	3846	CA	ASN	509	37.231	41.729	55.161	0.01	79.46
ATOM	3847	CB	ASN	509	37.748	40.301	54.959	0.01	79.66
ATOM	3848	CG	ASN	509	36.706	39.434	54.544	0.01	79.80
ATOM	3849	C	ASN	509	35.994	41.690	56.048	0.01	80.03
ATOM	3850	O	ASN	509	35.706	40.669	56.672	0.01	80.13
ATOM	3851	N	ASP	510	35.256	42.796	56.081	0.01	80.55
ATOM	3852	CA	ASP	510	34.042	42.894	56.885	0.01	81.01
ATOM	3853	CB	ASP	510	32.979	41.945	56.341	0.01	81.12
ATOM	3854	C	ASP	510	34.333	42.570	58.343	0.01	81.22
ATOM	3855	O	ASP	510	34.135	43.457	59.200	0.01	81.38
ATOM	3856	OXT	ASP	510	34.756	41.429	58.608	0.01	81.41
ATOM	3857	OH2	WAT	601	66.524	30.665	42.494	1.00	28.61
ATOM	3858	OH2	WAT	602	48.735	23.280	22.419	1.00	71.18
ATOM	3859	OH2	WAT	603	65.388	13.447	32.927	1.00	57.63
ATOM	3860	OH2	WAT	604	41.973	47.301	64.542	1.00	35.83
ATOM	3861	OH2	WAT	605	69.684	31.298	45.975	1.00	26.09
ATOM	3862	OH2	WAT	606	63.686	41.502	49.027	1.00	33.31
ATOM	3863	OH2	WAT	607	59.703	43.909	47.356	1.00	39.87
ATOM	3864	OH2	WAT	608	57.621	15.652	21.616	1.00	48.33
ATOM	3865	OH2	WAT	609	72.561	35.414	45.496	1.00	41.23
ATOM	3866	OH2	WAT	610	60.694	29.164	22.844	1.00	40.92
ATOM	3867	OH2	WAT	611	57.286	37.916	62.350	1.00	30.64
ATOM	3868	OH2	WAT	612	46.597	49.739	51.334	1.00	23.74
ATOM	3869	OH2	WAT	613	66.260	35.222	49.508	1.00	30.53
ATOM	3870	OH2	WAT	614	65.596	48.769	43.073	1.00	47.24
ATOM	3871	OH2	WAT	615	50.445	34.432	40.487	1.00	49.48
ATOM	3872	OH2	WAT	616	64.437	47.570	62.680	1.00	39.37
ATOM	3873	OH2	WAT	617	64.474	34.466	36.845	1.00	49.08
ATOM	3874	OH2	WAT	618	44.017	32.385	41.614	1.00	53.85
ATOM	3875	OH2	WAT	619	49.339	30.195	12.563	1.00	42.42
ATOM	3876	OH2	WAT	620	54.537	33.867	42.583	1.00	37.72
ATOM	3877	OH2	WAT	621	64.364	53.511	57.998	1.00	38.10
ATOM	3878	OH2	WAT	622	76.463	9.761	42.429	1.00	57.34
ATOM	3879	OH2	WAT	623	70.186	16.762	34.786	1.00	43.49
ATOM	3880	OH2	WAT	624	79.053	23.302	19.458	1.00	59.95
ATOM	3881	OH2	WAT	625	47.646	54.357	48.883	1.00	46.72
ATOM	3882	OH2	WAT	626	56.831	53.403	65.052	1.00	46.20
ATOM	3883	OH2	WAT	627	59.570	19.307	44.131	1.00	34.57
ATOM	3884	OH2	WAT	628	59.681	48.082	63.468	1.00	38.16
ATOM	3885	OH2	WAT	629	66.403	51.834	57.456	1.00	37.88
ATOM	3886	OH2	WAT	630	66.042	43.477	41.897	1.00	47.27
ATOM	3887	OH2	WAT	631	59.733	22.694	19.076	1.00	39.36
ATOM	3888	OH2	WAT	632	71.933	32.168	53.584	1.00	51.96
ATOM	3889	OH2	WAT	633	67.238	29.817	55.382	1.00	39.02
ATOM	3890	OH2	WAT	634	59.851	33.676	40.899	1.00	45.95
ATOM	3891	OH2	WAT	635	83.739	22.332	45.520	1.00	50.48
ATOM	3892	OH2	WAT	636	61.181	20.281	41.584	1.00	42.52
ATOM	3893	OH2	WAT	637	61.537	40.611	38.196	1.00	40.98
ATOM	3894	OH2	WAT	638	61.615	29.853	19.905	1.00	52.46
ATOM	3895	OH2	WAT	639	59.028	54.089	61.722	1.00	40.76
ATOM	3896	OH2	WAT	640	43.735	38.307	-3.516	1.00	60.92
ATOM	3897	OH2	WAT	641	55.950	37.085	38.131	1.00	48.00
ATOM	3898	OH2	WAT	642	55.110	41.451	65.214	1.00	32.81
ATOM	3899	OH2	WAT	643	61.727	25.862	29.188	1.00	46.24
ATOM	3900	OH2	WAT	644	65.928	18.150	38.925	1.00	40.13

ATOM	3901	OH2	WAT	645	55.177	34.966	24.691	1.00	46.33
ATOM	3902	OH2	WAT	646	41.487	51.896	47.974	1.00	65.65
ATOM	3903	OH2	WAT	647	55.395	15.492	23.549	1.00	56.95
ATOM	3904	OH2	WAT	648	59.898	21.613	26.137	1.00	33.49
ATOM	3905	OH2	WAT	649	58.699	47.923	70.573	1.00	54.29
ATOM	3906	OH2	WAT	650	64.003	58.536	60.177	1.00	49.67
ATOM	3907	OH2	WAT	651	68.010	11.136	22.922	1.00	46.58
ATOM	3908	OH2	WAT	652	55.678	50.674	68.586	1.00	46.85
ATOM	3909	OH2	WAT	653	45.897	25.870	27.002	1.00	57.96
ATOM	3910	OH2	WAT	654	54.359	26.790	48.758	1.00	66.55
ATOM	3911	OH2	WAT	655	80.363	16.850	38.325	1.00	34.34
ATOM	3912	OH2	WAT	656	61.431	53.904	60.446	1.00	58.46
ATOM	3913	OH2	WAT	657	64.395	35.461	52.723	1.00	35.60
ATOM	3914	OH2	WAT	658	52.526	40.800	64.728	1.00	50.80
ATOM	3915	OH2	WAT	659	56.877	31.825	56.618	1.00	45.68
ATOM	3916	OH2	WAT	660	55.868	27.878	30.041	1.00	53.59
ATOM	3917	OH2	WAT	661	77.776	15.905	45.073	1.00	59.14
ATOM	3918	OH2	WAT	662	63.754	25.151	14.194	1.00	46.52
ATOM	3919	OH2	WAT	663	41.878	53.249	63.058	1.00	44.80
ATOM	3920	OH2	WAT	664	80.591	16.000	36.009	1.00	51.39
ATOM	3921	OH2	WAT	665	59.393	45.412	72.211	1.00	77.96
ATOM	3922	OH2	WAT	666	51.497	25.366	16.022	1.00	38.80
ATOM	3923	OH2	WAT	667	61.863	12.713	17.304	1.00	43.79
ATOM	3924	OH2	WAT	668	63.503	14.941	33.560	1.00	42.89
ATOM	3925	OH2	WAT	669	61.973	36.087	65.135	1.00	50.06
ATOM	3926	OH2	WAT	670	53.296	56.350	56.050	1.00	44.60
ATOM	3927	OH2	WAT	671	59.130	10.280	24.662	1.00	48.60
ATOM	3928	OH2	WAT	672	78.580	23.713	47.588	1.00	55.99
ATOM	3929	OH2	WAT	673	56.562	19.517	13.895	1.00	44.27
ATOM	3930	OH2	WAT	674	65.541	48.376	65.243	1.00	65.80
ATOM	3931	OH2	WAT	675	68.517	47.817	50.926	1.00	51.64
ATOM	3932	OH2	WAT	676	52.940	45.320	33.774	1.00	66.09
ATOM	3933	OH2	WAT	677	75.668	19.068	52.383	1.00	57.66
ATOM	3934	OH2	WAT	678	70.723	37.503	60.123	1.00	46.72
ATOM	3935	OH2	WAT	679	50.335	33.290	18.844	1.00	45.69
ATOM	3936	OH2	WAT	680	52.500	32.843	54.796	1.00	53.72
ATOM	3937	OH2	WAT	681	57.066	23.070	13.074	1.00	50.65
ATOM	3938	OH2	WAT	682	61.915	33.379	63.218	1.00	48.04
ATOM	3939	OH2	WAT	683	67.948	43.379	49.661	1.00	44.42
ATOM	3940	OH2	WAT	684	57.359	22.912	26.139	1.00	41.68
ATOM	3941	OH2	WAT	685	79.814	28.506	19.445	1.00	49.19
ATOM	3942	OH2	WAT	686	74.126	12.870	30.657	1.00	42.03
ATOM	3943	OH2	WAT	687	49.421	21.379	14.426	1.00	61.74
ATOM	3944	OH2	WAT	688	66.525	36.888	51.906	1.00	42.72
ATOM	3945	OH2	WAT	689	82.488	11.904	44.349	1.00	51.00
ATOM	3946	OH2	WAT	690	73.678	42.567	41.135	1.00	56.59
ATOM	3947	OH2	WAT	691	55.539	33.853	27.113	1.00	58.89
ATOM	3948	OH2	WAT	692	44.960	47.684	36.358	1.00	58.30
ATOM	3949	OH2	WAT	693	63.736	54.302	65.440	1.00	63.02
ATOM	3950	OH2	WAT	694	48.109	58.899	55.284	1.00	55.29
ATOM	3951	OH2	WAT	695	45.345	35.120	-1.208	1.00	60.11
ATOM	3952	OH2	WAT	696	58.248	26.866	28.828	1.00	46.10
ATOM	3953	OH2	WAT	697	66.972	48.406	56.023	1.00	38.88
ATOM	3954	OH2	WAT	698	67.380	47.152	45.433	1.00	46.93
ATOM	3955	OH2	WAT	699	54.190	24.235	12.345	1.00	43.07
ATOM	3956	OH2	WAT	700	82.014	37.287	31.826	1.00	49.62
ATOM	3957	OH2	WAT	701	72.612	9.107	14.973	1.00	63.48
ATOM	3958	OH2	WAT	702	60.555	29.814	25.951	1.00	49.47
ATOM	3959	OH2	WAT	703	67.063	39.237	50.605	1.00	64.66
ATOM	3960	OH2	WAT	704	84.336	13.624	49.262	1.00	78.36
ATOM	3961	OH2	WAT	705	48.431	55.687	34.738	1.00	57.72

ATOM	3962	OH2	WAT	706	71.691	37.538	29.164	1.00	48.64
ATOM	3963	OH2	WAT	707	60.252	65.177	41.763	1.00	57.87
ATOM	3964	OH2	WAT	708	61.977	18.461	29.063	1.00	53.49
ATOM	3965	OH2	WAT	709	77.177	25.254	19.532	1.00	84.59
ATOM	3966	OH2	WAT	710	52.321	48.027	67.553	1.00	44.06
ATOM	3967	OH2	WAT	711	55.147	47.193	34.020	1.00	62.19
ATOM	3968	OH2	WAT	712	47.265	40.316	39.544	1.00	53.27
ATOM	3969	OH2	WAT	713	64.134	61.597	36.364	1.00	61.55
ATOM	3970	OH2	WAT	714	45.208	24.605	18.377	1.00	48.53
ATOM	3971	OH2	WAT	715	48.252	61.583	44.775	1.00	59.25
ATOM	3972	OH2	WAT	716	74.802	15.285	29.771	1.00	50.29
ATOM	3973	OH2	WAT	717	55.024	47.905	68.582	1.00	45.87
ATOM	3974	OH2	WAT	718	67.997	16.025	14.692	1.00	57.23
ATOM	3975	OH2	WAT	719	52.457	50.945	71.009	1.00	53.06
ATOM	3976	OH2	WAT	720	47.846	40.861	69.090	1.00	67.31
ATOM	3977	OH2	WAT	721	60.706	31.257	56.916	1.00	60.88
ATOM	3978	OH2	WAT	722	65.455	41.843	50.751	1.00	40.91
ATOM	3979	OH2	WAT	723	57.205	29.454	54.969	1.00	47.67
ATOM	3980	OH2	WAT	724	67.371	61.279	47.906	1.00	61.63
ATOM	3981	OH2	WAT	725	42.132	44.861	54.036	1.00	72.42
ATOM	3982	OH2	WAT	726	49.901	45.638	59.964	1.00	58.08
ATOM	3983	OH2	WAT	727	78.431	30.042	52.188	1.00	54.52
ATOM	3984	OH2	WAT	728	67.232	20.133	17.586	1.00	48.39
ATOM	3985	OH2	WAT	729	56.846	21.629	28.220	1.00	66.25
ATOM	3986	OH2	WAT	731	66.550	67.628	45.297	1.00	61.99
ATOM	3987	OH2	WAT	732	42.679	47.745	68.650	1.00	59.22
ATOM	3988	OH2	WAT	733	59.753	54.875	64.155	1.00	46.18
ATOM	3989	OH2	WAT	734	69.441	41.606	48.205	1.00	56.13
ATOM	3990	OH2	WAT	735	54.860	31.772	59.102	1.00	52.80
ATOM	3991	C1	NAG	911	72.132	24.580	59.897	1.00	88.45
ATOM	3992	C2	NAG	911	71.432	23.893	61.092	1.00	90.78
ATOM	3993	N2	NAG	911	70.376	23.011	60.624	1.00	92.23
ATOM	3994	C7	NAG	911	70.502	21.689	60.728	1.00	93.50
ATOM	3995	O7	NAG	911	71.152	21.141	61.623	1.00	93.42
ATOM	3996	C8	NAG	911	69.801	20.845	59.672	1.00	93.63
ATOM	3997	C3	NAG	911	70.831	24.939	62.047	1.00	91.07
ATOM	3998	O3	NAG	911	70.344	24.295	63.218	1.00	90.85
ATOM	3999	C4	NAG	911	71.879	25.985	62.436	1.00	91.28
ATOM	4000	O4	NAG	911	71.274	27.004	63.221	1.00	91.82
ATOM	4001	C5	NAG	911	72.494	26.594	61.170	1.00	91.20
ATOM	4002	O5	NAG	911	73.089	25.551	60.360	1.00	90.01
ATOM	4003	C6	NAG	911	73.588	27.607	61.477	1.00	91.15
ATOM	4004	O6	NAG	911	73.105	28.667	62.292	1.00	89.63
ATOM	4005	C1	NAG	941	94.155	27.124	39.668	1.00	83.74
ATOM	4006	C2	NAG	941	93.682	28.571	39.467	1.00	85.78
ATOM	4007	N2	NAG	941	92.491	28.591	38.639	1.00	87.29
ATOM	4008	C7	NAG	941	91.434	29.308	39.013	1.00	87.84
ATOM	4009	O7	NAG	941	90.910	29.191	40.121	1.00	88.39
ATOM	4010	C8	NAG	941	90.882	30.316	38.016	1.00	87.53
ATOM	4011	C3	NAG	941	94.793	29.413	38.819	1.00	87.28
ATOM	4012	O3	NAG	941	94.397	30.779	38.775	1.00	87.44
ATOM	4013	C4	NAG	941	96.097	29.280	39.622	1.00	88.25
ATOM	4014	O4	NAG	941	97.156	29.948	38.945	1.00	88.64
ATOM	4015	C5	NAG	941	96.450	27.795	39.806	1.00	88.22
ATOM	4016	O5	NAG	941	95.356	27.100	40.454	1.00	85.86
ATOM	4017	C6	NAG	941	97.695	27.577	40.652	1.00	88.36
ATOM	4018	O6	NAG	941	97.384	27.551	42.038	1.00	88.02
ATOM	4019	C1	NAG	951	54.055	18.637	25.913	1.00	63.88
ATOM	4020	C2	NAG	951	55.035	17.683	26.604	1.00	64.92
ATOM	4021	N2	NAG	951	56.133	17.389	25.708	1.00	62.42
ATOM	4022	C7	NAG	951	57.321	17.936	25.923	1.00	61.61

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ATOM   4023  O7  NAG   951      57.488  18.897  26.673  1.00 61.97
ATOM   4024  C8  NAG   951      58.507  17.323  25.201  1.00 62.25
ATOM   4025  C3  NAG   951      54.326  16.379  27.003  1.00 68.63
ATOM   4026  O3  NAG   951      55.206  15.566  27.768  1.00 66.57
ATOM   4027  C4  NAG   951      53.057  16.687  27.814  1.00 71.99
ATOM   4028  O4  NAG   951      52.327  15.468  28.079  1.00 78.42
ATOM   4029  C5  NAG   951      52.178  17.671  27.024  1.00 70.23
ATOM   4030  O5  NAG   951      52.923  18.877  26.751  1.00 66.53
ATOM   4031  C6  NAG   951      50.911  18.086  27.746  1.00 69.73
ATOM   4032  O6  NAG   951      49.903  18.488  26.828  1.00 68.69
ATOM   4033  C1  NAG   952      52.203  15.123  29.418  1.00 84.50
ATOM   4034  C2  NAG   952      50.843  14.467  29.674  1.00 87.78
ATOM   4035  N2  NAG   952      49.773  15.386  29.332  1.00 88.99
ATOM   4036  C7  NAG   952      49.117  15.239  28.184  1.00 90.08
ATOM   4037  O7  NAG   952      49.630  14.740  27.176  1.00 90.89
ATOM   4038  C8  NAG   952      47.670  15.708  28.144  1.00 90.00
ATOM   4039  C3  NAG   952      50.744  14.054  31.149  1.00 89.39
ATOM   4040  O3  NAG   952      49.530  13.345  31.371  1.00 90.01
ATOM   4041  C4  NAG   952      51.934  13.163  31.527  1.00 90.10
ATOM   4042  O4  NAG   952      51.910  12.898  32.925  1.00 92.36
ATOM   4043  C5  NAG   952      53.256  13.853  31.148  1.00 89.28
ATOM   4044  O5  NAG   952      53.253  14.204  29.745  1.00 86.82
ATOM   4045  C6  NAG   952      54.470  12.971  31.390  1.00 88.91
ATOM   4046  O6  NAG   952      54.846  12.275  30.211  1.00 89.44
END
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Claims

1. A method for identifying a potential modulator compound for ErbB2 which method comprises:

(a) providing a three-dimensional structure of

(i) amino acids 1-509 of ErbB2 polypeptide having the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or

(ii) a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I;

(b) providing the three-dimensional structure of a candidate compound;

(c) assessing the stereochemical complementarity between the three-dimensional structure of step (b) and a region of the three-dimensional structure of step (a); and

(d) selecting a compound on the basis of the stereochemical complementarity.

2. A method as claimed in claim 1, which further comprises:

(e) synthesising or obtaining a candidate compound assessed in step (c) as possessing stereochemical complementarity with a topographical region of the three-dimensional structure of step (a);

(f) determining the ability of the candidate compound to interact with and/or modulate the activity of ErbB2.

3. A method as claimed in claim 1 or claim 2, wherein the subset of amino acids is selected from at least one of the CR1 domain, the potential CR1 loop docking site between the L1, CR1 and L2 domains, the CR1-L2 hinge region, the regions of the L1 and L2 domains that contact each other in a closed conformation.

4. A method as claimed in any one of the preceding claims, wherein the subset of amino acids defines at least a part of the heterodimerisation surface with another member of the EGF receptor family.

5. A method as claimed in claim 4, wherein the member of the EGF receptor family is selected from the group consisting of ErbB1 (EGF receptor), ErbB3 and ErbB4.

6. A method as claimed in claim 4 or 5, wherein the heterodimerisation surface includes at least one of (i) the N-terminal end of the CR1 domain, (ii) the CR1 domain dimerisation loop and adjacent residues and (iii) the C-terminal end of the CR1 domain.

7. A method according to claim 6, wherein the surface comprises at least one of residues selected from 200-203, 210-213, 216-218, 225-230, 247-268, 244-246, 285-289) and 294-319.

8. A method as claimed in claim 3, wherein the subset defines the CR1 loop docking site.

9. A method as claimed in claim 8, wherein the docking site comprises at least one of the following ErbB2 residues: Gln 36, Gln 60, Arg 82, Thr 84, Gln 85, Phe 237, Thr 269, Phe 270, Gly 271, Ala 272, Tyr 282, Thr 285, Gly 288, Ser 289, Cys 290, Thr 291, Leu 292, Val 293, Cys 294, Pro 295 and Cys 310.

10. A method as claimed in any one of the preceding claims wherein the method is performed *in silico*.

11. A method as claimed in claim 10, wherein the candidate compound is selected from a real compound, a virtual compound or a combination thereof.

12. A method as claimed in claim 10 or 11, wherein the compound is in a library with at least one other candidate compound.

13. A method as claimed in any one of claims 10 to 12, wherein the method is used for targeted screening.

14. A method as claimed in any one of claims 10 to 12, wherein the library comprises an array of maximally diverse compounds.

15. A method of modulating ErbB2, the method comprising contacting the receptor with a compound that matches a region selected from at least one of the CR1 domain, the potential CR1 loop docking site between the L1, CR1 and L2 domains, the CR1-L2 hinge region, and the regions of the L1 and L2 domains that contact each other in a closed conformation.

16. A method as claimed in claim 15, wherein the region is a heterodimerisation surface of the receptor with another member of the EGF receptor family.

17. A method according to claim 16, wherein the other member of the EGF receptor family is selected from the group consisting of ErbB1 (EGF receptor), ErbB3 and ErbB4.

18. A method as claimed in claim 16 or 17, wherein the heterodimerisation surface includes at least one of (i) the N-terminal end of the CR1 domain, (ii) the CR1 domain dimerisation loop and adjacent residues and (iii) the C-terminal end of the CR1 domain.

19. A method according to claim 18, wherein the surface comprises at least one of residues selected from 200-203, 210-213, 216-218, 225-230, 247-268, 244-246, 285-289) and 294-319.

20. A method as claimed in claim 16 or claim 17, wherein the region is the CR1 loop docking site.

21. A method as claimed in claim 20, wherein the region comprises at least one of the following ErbB2 residues: Gln 36, Gln 60, Arg 82, Thr 84, Gln 85, Phe 237, Thr 269, Phe 270, Gly 271, Ala 272, Tyr 282, Thr 285, Gly 288, Ser 289, Cys 290, Thr 291, Leu 292, Val 293, Cys 294, Pro 295 and Cys 310.

22. A method as claimed in any one of claims 15 to 21, wherein the molecule is a small molecule modulator.

23. A method as claimed in claim 22, wherein the small molecule is identified by the method of claim 1.

24. A method according to any one of claims 15 to 21, wherein the molecule is an antibody.

25. A computer-based method of identifying a candidate modulator of ErbB2, which method comprises fitting the structure of

(a) amino acids 1-509 of ErbB2 polypeptide having the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or

(b) a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I;

to the structure of a candidate modulator molecule.

26. A computer-assisted method for identifying candidate compounds able to interact with ErbB2 and thereby modulate an activity mediated by the receptor, using a programmed computer comprising a processor, an input device, and an output device, which method comprises the steps of:

(a) entering into the programmed computer, through the input device, data comprising the atomic coordinates of amino acids 1-509 of ErbB2 as shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I, or a subset of said coordinates;

(b) generating, using computer methods, a set of atomic coordinates of a structure that possesses stereochemical complementarity to the atomic coordinates entered in step (a), thereby generating a criteria data set;

(c) comparing, using the processor, the criteria data set to a computer database of chemical structures;

(d) selecting from the database, using computer methods, chemical structures which are similar to a portion of said criteria data set; and

(e) outputting, to the output device, the selected chemical structures which are complementary to or similar to a portion of the criteria data set.

27. A method for evaluating the ability of a candidate modulator to interact with ErbB2, said method comprising the steps of:

(a) providing a computer model of at least one region of ErbB2 using structure coordinates wherein the root mean square deviation between said structure coordinates and the structure coordinates of amino acids 1-509 of ErbB2 as set forth in Appendix I is not more than 1.5 Å;

(b) employing computational means to perform a fitting operation between the chemical entity and said computer model of the binding surface; and

(c) analysing the results of said fitting operation to quantify the association between the chemical entity and the binding surface model.

28. A computer system for identifying one or more candidate modulators of ErbB2 , the system containing data representing the structure of

(a) amino acids 1-509 of ErbB2 polypeptide having the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or

(b) a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I.

29. A computer for producing a three-dimensional representation of a molecule or molecular complex, wherein the computer comprises:

(a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein the machine readable data comprises (i) the atomic coordinates of amino acids 1-509 of ErbB2 polypeptide as shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or (ii) the atomic coordinates of a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I;

(b) a working memory for storing instructions for processing the machine-readable data;

(c) a central-processing unit coupled to the working memory and to the machine-readable data storage medium, for processing the machine-readable data into the three dimensional representation; and

(d) an output hardware coupled to the central processing unit, for receiving the three-dimensional representation.

30. A computer readable media having recorded thereon data representing a model and/or the atomic coordinates of a ErbB2 crystal.

31. A computer readable media having recorded thereon coordinate data according to Appendix I, or a subset thereof, where said coordinate data define a three dimensional structure of amino acids 1-509 of ErbB2 polypeptide or a subset of said amino acids, or coordinate data having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinate according to Appendix I, or a subset thereof.

32. A crystal of ErbB2 polypeptide.

33. A crystal of ErbB2 polypeptide having a space group $P2_12_12_1$ with unit cell dimensions of a=75.96 Å, b=82.24 Å, and c=110.06 Å, with up to about 1% variation in any cell dimension

34. A crystalline composition comprising a crystal of ErbB2.

35. A method of using molecular replacement to obtain structural information about a molecule or a molecular complex of unknown structure, comprising the steps of:

(a) crystallising said molecule or molecular complex;

(b) generating an X-ray diffraction pattern from said crystallized molecule or molecular complex;

(c) applying at least a portion of the structure coordinates set forth in Appendix I, or structure coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the structure coordinates set forth in Appendix I, to the X-ray diffraction

pattern to generate a three-dimensional electron density map of at least a portion of the molecule or molecular complex whose structure is unknown.

36. A method according to claim 35 wherein the molecule of unknown structure is ErbB2 or variant thereof.

37. A method according to claim 36 wherein the molecular complex of unknown structure is a complex of ErbB2 and an EGF receptor.

38. A method according to claim 37 wherein the molecular complex of unknown structure is a complex of ErbB2, an ErbB1, ErbB3 or ErbB4 receptor and a ligand or candidate ligand.

39. A method for preventing or treating a disease associated with signaling by ErbB2 which method comprises administering to a subject in need thereof a compound identified by the method of any one of claims 1 to 27.

40. A pharmaceutical composition comprising a compound identified by the method of any one of claims 1 to 27.

41. A method for preparing a pharmaceutical composition for treating diseases associated with aberrant ErbB2 signalling, the method comprising:

(a) providing a three-dimensional structure of

(i) amino acids 1-509 of ErbB2 polypeptide having the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I; or

(ii) a subset of said amino acids having a corresponding subset of the atomic coordinates shown in Appendix I, or atomic coordinates having a root mean square deviation of backbone atoms of not more than 1.5Å when superimposed on the corresponding backbone atoms described by the atomic coordinates shown in Appendix I;

(b) providing the three-dimensional structure of a candidate compound;

(c) assessing the stereochemical complementarity between the three-dimensional structure of step (b) and a region of the three-dimensional structure of step (a); and

(d) selecting a compound on the basis of the stereochemical complementarity;

(e) synthesising or obtaining a candidate compound assessed in step (c) as possessing stereochemical complementarity with the three-dimensional structure of step (a);

(f) determining the ability of the candidate compound to interact with and/or modulate the activity of ErbB2; and

(g) incorporating the compound into a pharmaceutical composition.

42. A method of preventing or treating a disease associated with signalling by ErbB2 which method comprises administering to a subject in need thereof a composition according to claim 40.

43. An antibody that binds to ErbB2, the antibody being directed against at least one of the N-terminal end of the CR1 domain, the CR1 domain dimerisation loop and adjacent residues and the C-terminal end of the CR1 domain.

44. An antibody as claimed in claim 43, the antibody being directed against a structure defined by (i) ErbB2 amino acid residues 200-203, (ii) ErbB2 amino acid residues 210-213, (iii) ErbB2 amino acid residues 216-218, (iv) ErbB2 amino acid residues 225-230, (v) ErbB2 amino acid residues 247-268 or a subset thereof; (vi) ErbB2 amino acid residues 244-246, (vii) ErbB2 amino acid residues 285-289, or (viii) ErbB2 amino acid residues 294-319 or a subset thereof.

45. An isolated conformationally constrained peptide or peptidomimetic consisting essentially of (i) ErbB2 amino acid residues 200-203, (ii) ErbB2 amino acid residues 210-213, (iii) ErbB2 amino acid residues 216-218, (iv) ErbB2 amino acid residues 225-230, (v) ErbB2 amino acid residues 247-268 or a subset thereof; (vi) ErbB2 amino acid residues 244-246, (vii) ErbB2 amino acid residues 285-289, or (viii) ErbB2 amino acid residues 294-319 or a subset thereof.

46. An *in vitro* assay for identifying a potential modulator compound for ErbB2 the method comprising contacting a candidate compound with a CR1 domain dimerisation loop or fragment thereof and determining whether the compound binds to the dimerisation loop or fragment thereof.

Title: CRYSTAL STRUCTURE OF ERBB2 AND USES THEREOF

Inventor(s): Thomas Peter John GARRETT et al.

Appl. No.: Unassigned

10/529887

WO 2004/031232

PCT/AU2003/001310

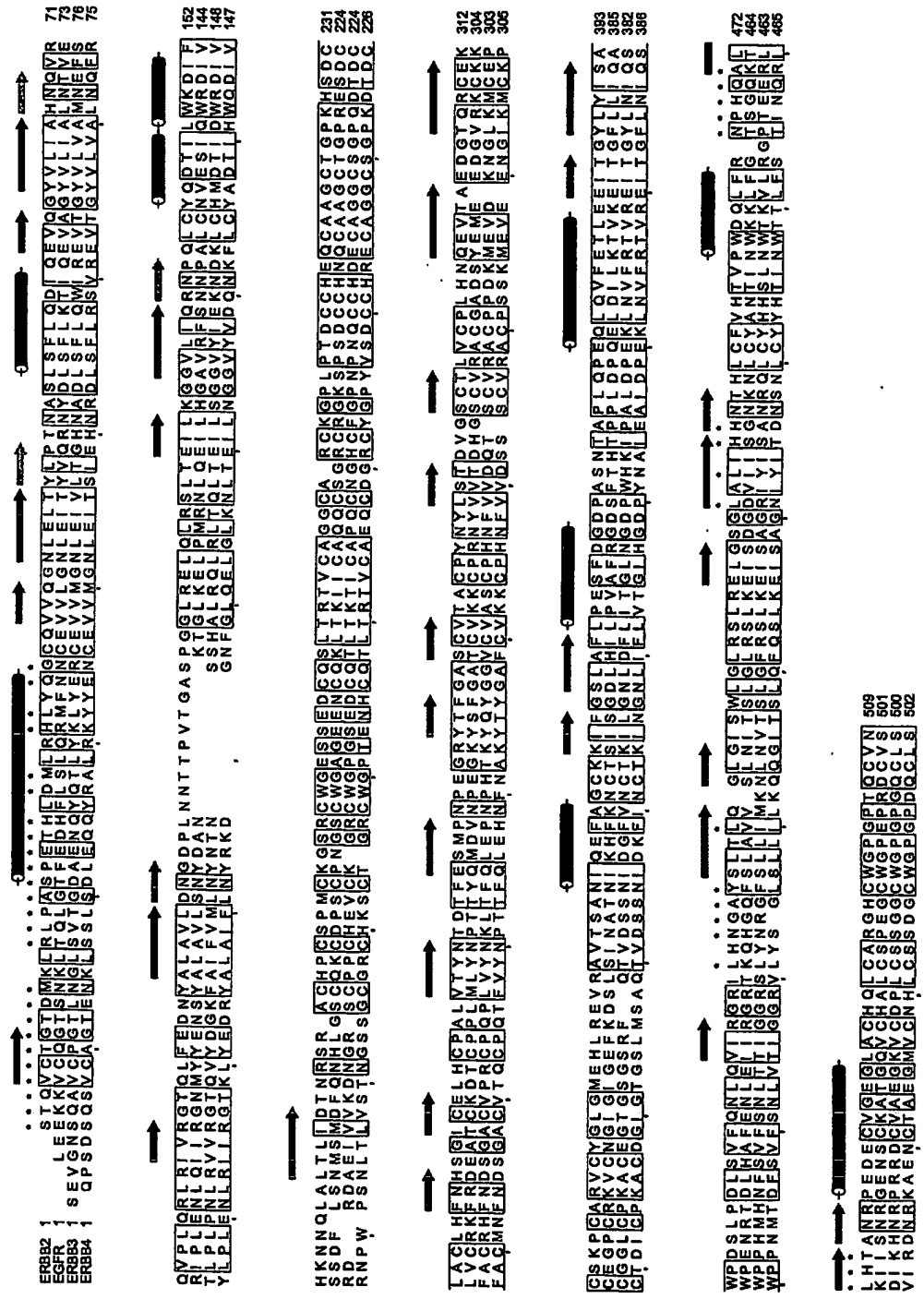


Figure 1

Title: CRYSTAL STRUCTURE OF ERBB2 AND USES THEREOF
Inventor(s): Thomas Peter John GARRETT et al.
Appl. No.: Unassigned
10/529887
WO 2004/031232
PCT/AU2003/001310

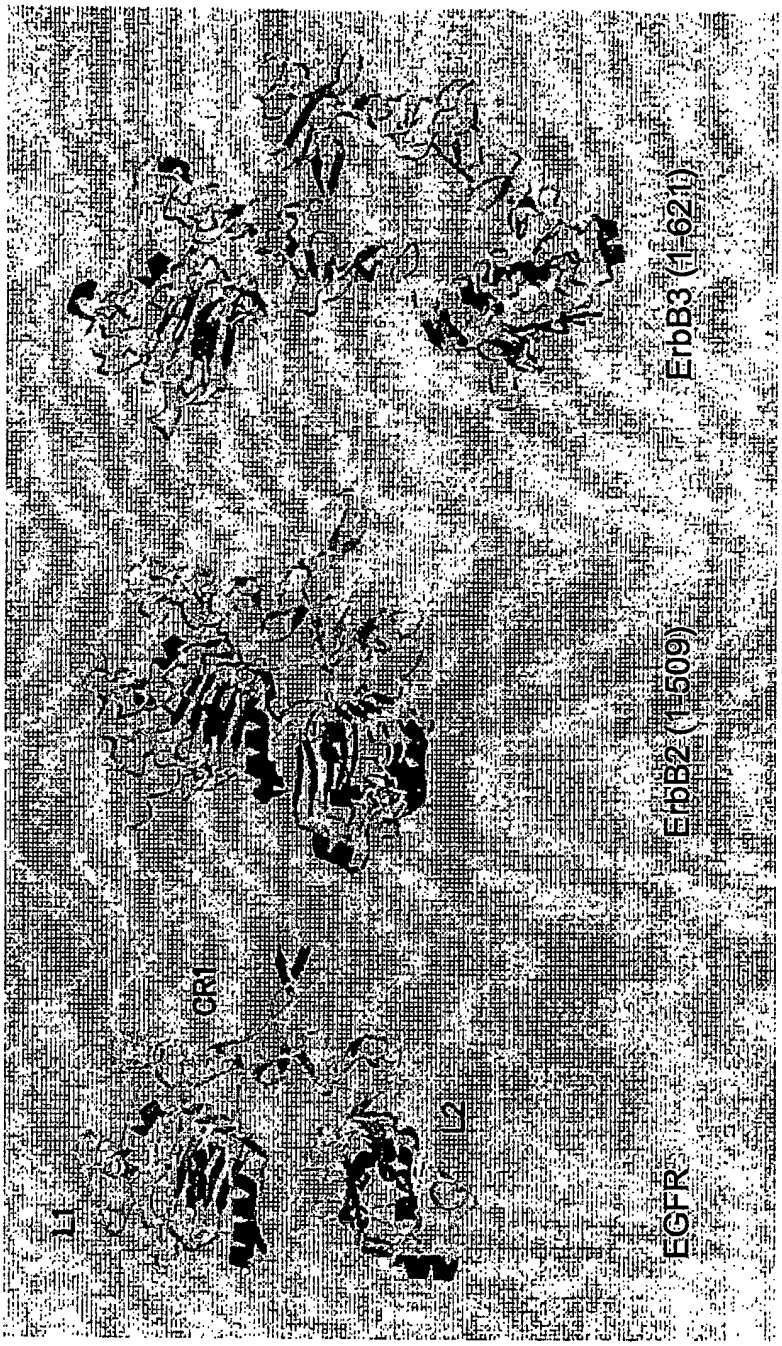
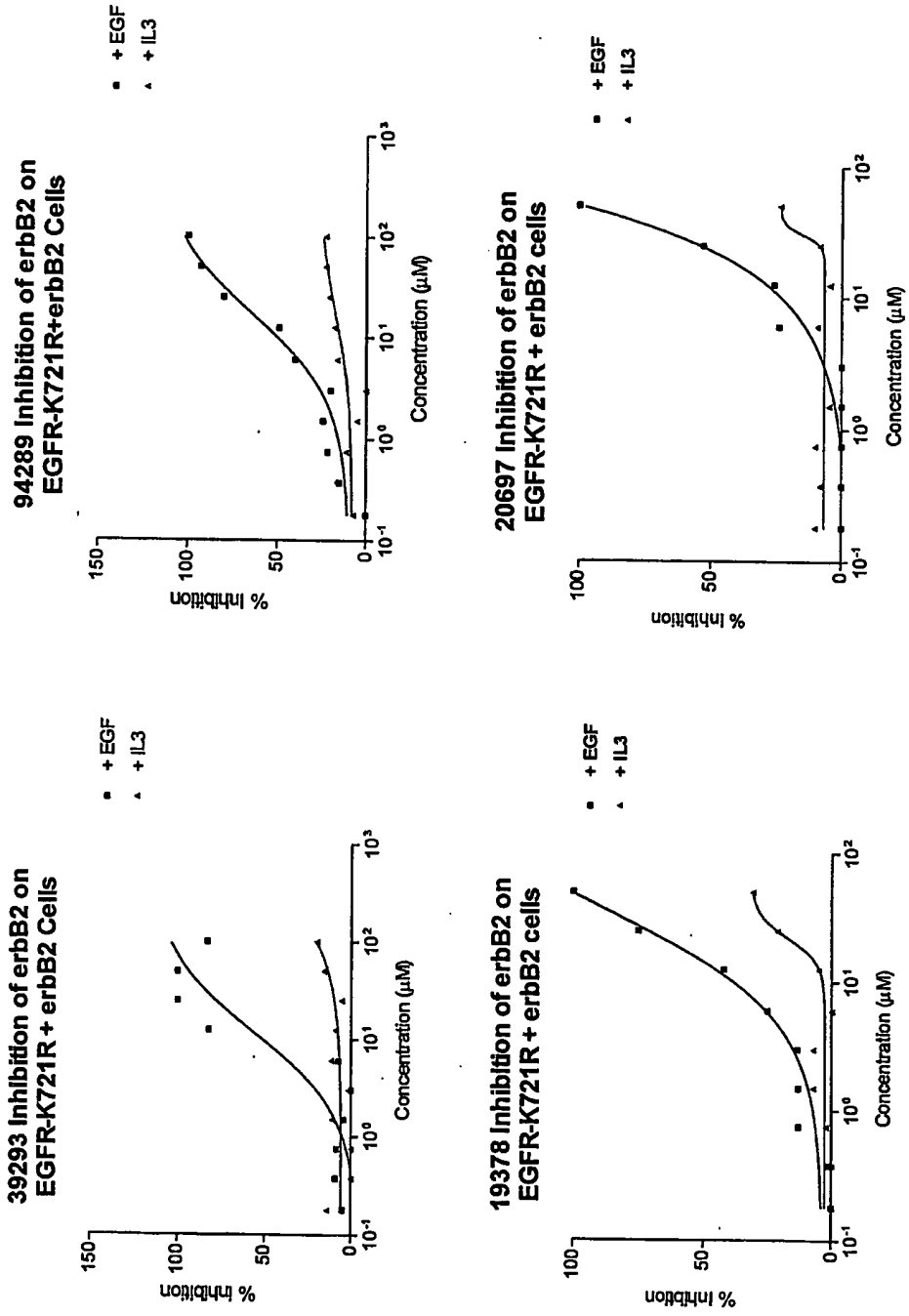


Figure 2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39293 Inhibition of erbB2 on EGFR-K721R + erbB2 Cells
19378 Inhibition of erbB2 on EGFR-K721R + erbB2 cells
+ EGF
+ IL3
% Inhibition
Concentration (µM)

Figure 3

JC Rec'd PCT/PTO 01 APR 2005

WO 2004/031232 PCT/AU2003/001310

SEQUENCE LISTING

<110> Commonwealth Scientific and Industrial Research Organisation
Walter and Eliza Hall Institute of Medical Research
Ludwig Institute for Cancer Research

<120> Crystal structure of ErbB2 and uses thereof

<130> 501742/JEP

<150> Australian Patent Provisional Application No 2002951853
<151> 2002-10-04

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Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys Ala Arg Cys Lys Gly
        195                 200                 205

Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr
    210                 215                 220

Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu His Phe Asn His Ser
225                 230                 235                 240

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Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala
            260                 265                 270

Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu Ser Thr Asp Val Gly
        275                 280                 285

Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln Glu Val Thr Ala Glu
    290                 295                 300

Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val
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Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr
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Asn Tyr Asp Leu Ser Phe Leu Lys Thr Ile Gln Glu Val Ala Gly Tyr
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Gly Ser Cys Gln Lys Cys Asp Pro Ser Cys Pro Asn Gly Ser Cys Trp
                165                 170                 175

Gly Ala Gly Glu Glu Asn Cys Gln Lys Leu Thr Lys Ile Ile Cys Ala
            180                 185                 190

Gln Gln Cys Ser Gly Arg Cys Arg Gly Lys Ser Pro Ser Asp Cys Cys
        195                 200                 205

His Asn Gln Cys Ala Ala Gly Cys Thr Gly Pro Arg Glu Ser Asp Cys
    210                 215                 220

Leu Val Cys Arg Lys Phe Arg Asp Glu Ala Thr Cys Lys Asp Thr Cys
225                 230                 235                 240

Pro Pro Leu Met Leu Tyr Asn Pro Thr Thr Tyr Gln Met Asp Val Asn
                245                 250                 255

Pro Glu Gly Lys Tyr Ser Phe Gly Ala Thr Cys Val Lys Lys Cys Pro
            260                 265                 270

Arg Asn Tyr Val Val Thr Asp His Gly Ser Cys Val Arg Ala Cys Gly
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Ala Asp Ser Tyr Glu Met Glu Glu Asp Gly Val Arg Lys Cys Lys Lys
    290                 295                 300
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Asn Cys Thr Ser Ile Ser Gly Asp Leu His Ile Leu Pro Val Ala Phe
            340                 345                 350

Arg Gly Asp Ser Phe Thr His Thr Pro Pro Leu Asp Pro Gln Glu Leu
        355                 360                 365

Asp Ile Leu Lys Thr Val Lys Glu Ile Thr Gly Phe Leu Leu Ile Gln
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Ile Ile Arg Gly Arg Thr Lys Gln His Gly Gln Phe Ser Leu Ala Val
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Ser Asp Gly Asp Val Ile Ile Ser Gly Asn Lys Asn Leu Cys Tyr Ala
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65                  70                  75                  80

Pro Asn Leu Arg Val Val Arg Gly Thr Gln Val Tyr Asp Gly Lys Phe
                85                  90                  95

Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser His Ala Leu
            100                 105                 110

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        115                 120                 125

Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr Ile Asp Trp
    130                 135                 140

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Gly Arg Ser Cys Pro Pro Cys His Glu Val Cys Lys Gly Arg Cys Trp
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Gly Pro Gly Ser Glu Asp Cys Gln Thr Leu Thr Lys Thr Ile Cys Ala
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Pro Gln Cys Asn Gly His Cys Phe Gly Pro Asn Pro Asn Gln Cys Cys
        195                 200                 205

His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp Thr Asp Cys
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Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val Pro Arg Cys
225                 230                 235                 240
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His Asn Phe Val Val Asp Gln Thr Ser Cys Val Arg Ala Cys Pro Pro
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Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys Glu Pro Cys
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Gly Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser Gly Ser Arg
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Lys Ile Leu Gly Asn Leu Asp Phe Leu Ile Thr Gly Leu Asn Gly Asp
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485 490 495

Pro Asp Gln Cys Leu Ser
500